JOURNAL OF GERONTOLOGY

Volume 3 JANUARY, 1948 Number 1

The Use of Drosophila Melanogaster as a Screening Agent for Longevity Factors.

I. Pantothenic Acid as a Longevity Factor in Royal Jelly.

THOMAS S. GARDNER

INVESTIGATING THE CHEMICAL COMPONENTS OF ROYAL JELLY, DR. GARDNER FOUND, USING DROSOPHILA MELANOGASTER AS THE TESTING MEDIUM, THAT PANTOTHENIC ACID WAS THE PRIMARY ANTI-AGING FACTOR AND THAT OTHER CHEMICAL COMPONENTS OF ROYAL JELLY HAD LITTLE OR EVEN DETRIMENTAL EFFECTS ON LONGEVITY.

HONEY and royal jelly in historic times have been associated with a long and healthy life to a greater extent than any other natural product. The mystery of the hive has captured the imagination of many writers (20). Bee larvae fed on royal jelly for their complete life cycle develop into the queen bees, while the worker bee larvae obtain it only the first few days of their life. The queen also receives royal jelly during the heavy egg laying periods. Queen bees live about five years, while the workers wear themselves out in a summer.

It is only natural that the food of the queen bee should receive notice as contributing to her longer life span, as well as her biologic role in the hive. Countless legends of the health and longevity of people who consume large quantities of honey and its products may be found in almost any book dealing with apiculture (2). Sometimes the longevity effects are ascribed to the pollen residues found in the hive (19). The effect of honey on the length of life has been reported to be under systematic investigation in the U.S.S.R. (38).

Royal jelly offers a line of attack for possible longevity factors and has been investigated in this report using Drosophila melanogaster as a test organism.

Royal jelly is a thick, viscous fluid with a flower-like odor presumably secreted by the pharyngeal glands of the young worker bees. The prolific egg production of the queen bee fed on royal jelly has suggested the presence of estrogenic hormones. Gonadotropic activity on rats was claimed by Heyl (15). This was immediately disputed by Melampy and Stanley (23). Although there was some doubt expressed as to the technique (36) of chemical separation of royal jelly for gonadotropic testing, the last investigations reported still leave the question in doubt; for example, Abbott (1) claims positive estrogenic results on spayed rats, while Stanley, Mickey, Melampy, and Oertel (35) just as strongly claim negative gonadotropic and estrogenic properties for white rats.

The discovery of the effect of Vitamin E on reproduction led to a further examination of royal jelly. At first, Vitamin E was reported (16), but subsequent reports from several independent investigators showed

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This paper was presented before the Division of Biological Chemistry at the New York meeting of the American Chemical Society in September, 1947.

Mr. Allen Latham, Norwichtown, Connecticut, and Mr. D. P. Green, Deland, Florida, supplied the royal jelly, and Dr. M. H. Harnly, Department of Zoology, Washington Square, New York, supplied the initial culture of D. melanogaster.

none or very little Vitamin E (8, 12, 21, 22, 28). Vitamin A (28) and C (14, 28) also seem to be practically absent. Royal jelly is a fair source of B_1 assaying an average of 9 μ g/g. on a dry basis (13, 14, 28).

However, royal jelly was found to be the richest known natural source of pantothenic acid (17, 28). Various samples of royal jelly gave average analyses of pantothenic acid of 500 μ g/g. on a dry basis. Kitzes, Schuette, and Elvehjem (17) in an extensive analysis using microbiologic assays on one sample of royal jelly obtained for pantothenic acid 320; B_2, 28; nicotinic acid, 111; B_6, 10-2; Biotin, 4.1, and folic acid 0.5 μ g/g. on a dry basis. The biotin content is also relatively very high compared to other natural sources. It is interesting to note that the concentration of pantothenic acid in royal jelly is about seventeen times greater than found in pollen, while the other B vitamins have about the same concentration in royal jelly and pollen (29).

The digestive coefficient of royal jelly in rats is 81 per cent and the average biologic value of the protein 75 per cent (22). Royal jelly has marked bacteriostatic and bacteriocidal properties (25) to Es. coli, and Eb. typhosia in 1 to 50 concentration, and Staphylococcus aureus and B. Metiens in 1 to 100. This activity resided in the alcohol, or acetone soluble fraction.

Most chemical analyses give overall data only; for example (22), total water, 66 per cent; protein, 12.34 per cent; total lipids, 5.46 per cent; total reducing substances, 12.4 per cent; ash, 0.82 per cent; and undetermined, 2.84 per cent. Fortunately, Townsend and Lucas (37) published a chemical separation of the various components of royal jelly. Their paper is the most important one on the chemical characterization of royal jelly and was used as the basis for this investigation.

Experimental

If there are chemical compounds in royal jelly that aid the queen bee to live longer than the hive workers, then it might be possible to get an extension of life span of a related form of life such as the fruit fly. It was desirable to use an experimental organism that would require only very small quantities of the different chemical fractions of royal jelly because of the small amounts available of some of the ether soluble fractions. The design of the experiment was such as to test each fraction separately and also over-all so as to screen out any compound or compounds that gave promise of being a longevity factor.

The fruit flies (Drosophila melanogaster oregon) used were a hardy strain. The culture medium consisted of 15 gm. of Fleischmann Yeast in 100 ml. of water which was boiled, and then 3 ml. of glacial acetic acid were added as a sterilizing agent (7). Ten ml. of the medium were added to sterile, 6-oz. bottles. Sufficient sterilized antiseptic-grade cotton was then pressed in the bottom of the bottles to take up excess moisture. The bottles were closed by tight cotton plugs. The test fractions of royal jelly were added in solution to the hot medium and then further sterilized at 100 C. for three minutes.

There was one exception. All tests on

pantothenic acid had the calcium pantothenate added in sterile, cold water to previously sterilized cold media. This was considered advisable because of the instability of free pantothenic acid to heat, and especially hot acid solutions. Pantothenic acid is such a good promoter for the growth of bacteria that it is necessary to use cultures practically bacteria free. Test cultures containing bacteria, although exhibiting differences in durations of life according to the test media, gave poorer results than cultures free or relatively free of pathogenic bacteria.

Sterilized yeast has been considered a complete medium for growth and development of Drosophila from egg to imago (18, 34). The effect of nutrient supplements of the vitamin type have not been investigated to date.

The fruit fly cultures were reared on a yeast-banana medium described by Loeb and Northrop (18). The newly emerged imagos were transferred to the test bottles and observed daily. Whenever imagos were about to emerge from pupae in the test bottles, the flies were transferred to fresh bottles of the same composition. Dates of deaths were recorded and an arithmetical average computed. Fifty to a 100 flies were used in ascertaining each average length of life. Ten to 15 flies were allowed to each bottle. The bottles were maintained at 30 C. because it has been shown that the length of life of fruit flies is a function of temperature (18). Northrop obtained 13 to 14 days as the average length of life of the fruit fly imagos at 30 C. for most of his cultures. A variation arose with some old cultures that gave a lower value, approximately 11 days.

The royal jelly was dried and separated

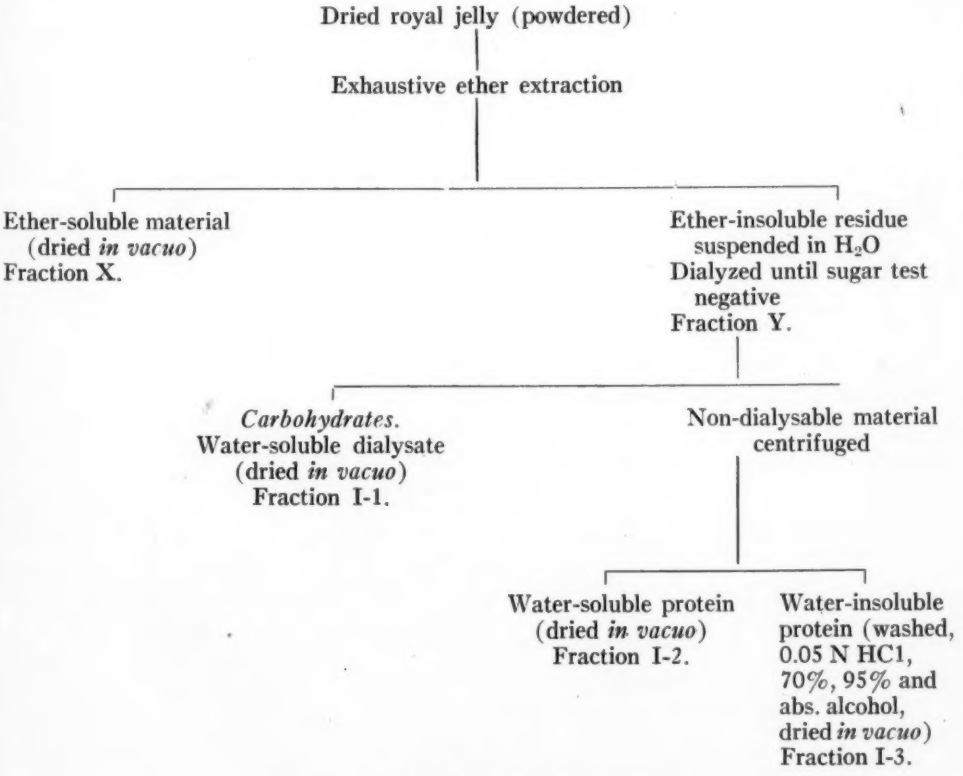
Dried royal jelly (powdered)
Exhaustive ether extraction
Ether-soluble material (dried *in vacuo*) Fraction X.
Ether-insoluble residue suspended in H_2O Dialyzed until sugar test negative Fraction Y.
Carbohydrates. Water-soluble dialysate (dried *in vacuo*) Fraction I-1.
Non-dialysable material centrifuged
Water-soluble protein (dried *in vacuo*) Fraction I-2.
Water-insoluble protein (washed, 0.05 N HC1, 70%, 95% and abs. alcohol, dried *in vacuo*) Fraction I-3.

FIGURE 1. (Adapted from Townsend and Lucas.)

by a chemical procedure previously published (37). Figures 1 and 2 illustrate the scheme used in this separation. The royal jelly fractions were stored under anhydrous conditions and appeared to be stable over a period of several months.

The combination of heat, alkaline extraction, and acidification used in the recovery of the acid fractions in the ether soluble portion of royal jelly destroyed most of the pantothenic acid present. Therefore the average pantothenic content of royal jelly (0.5 per cent) was used separately for testing its longevity effects.

Results

Figure 3 contains the data collected on the average length of life of fruit flies fed the various fractions of royal jelly and pantothenic acid. It will be observed that the average length of life of the controls, 13.3 days, falls within the range previously determined by Loeb and Northrop (18).

Dehydrated royal jelly has no effect in very small quantities, but a beneficial effect in large quantities. The over-all ether insoluble fraction (Y) has no effect on life span, but the over-all ether soluble fraction (X) decreases the average life span. The ether insoluble fractions (I-1, 2, 3) consisting of carbohydrates and proteins have no appreciable effect on the average life span in the quantities tested. The separated ether soluble fractions give different results according to their chemical composition.

Fractions S-1, 5, and 6, consisting of phenols, waxes, and phospholipids slightly decrease the average length of life, while fraction S-4, sterols and glycerides, has no effect. Fraction S-2, 3, consisting of the combined

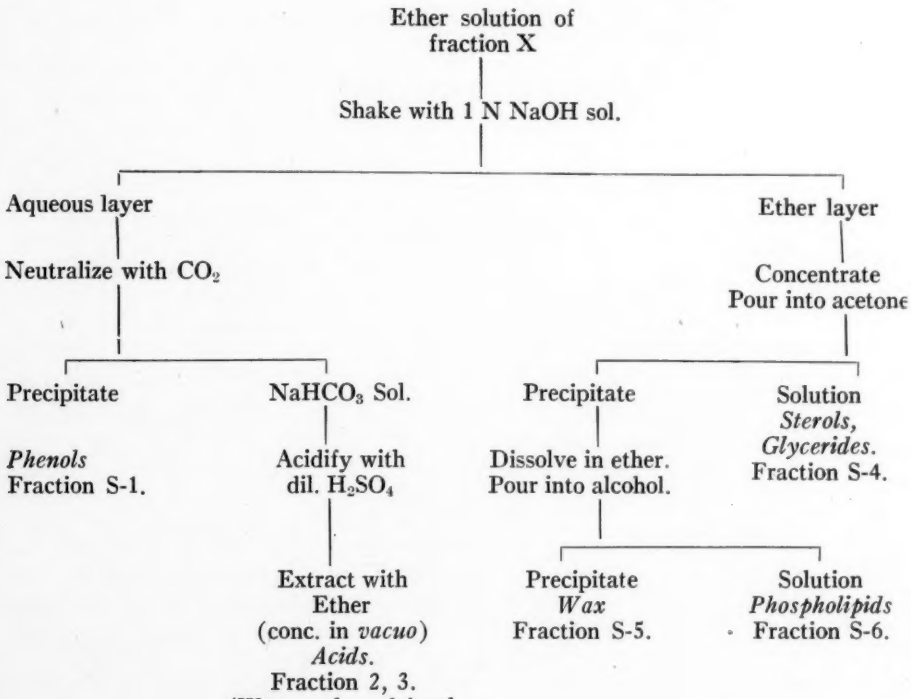

Figure 2. (Adapted from Townsend and Lucas.)

water soluble and insoluble organic acids, has no effect in small quantities but a beneficial effect in large quantities.

The decrease in length of life of some of the ether soluble fractions may be connected with previously observed bactericidal action of the ether soluble fractions of royal jelly (25), or even with the earlier maturity observed on fruit flies reared on the ether soluble fractions (36).

The beneficial effects of pantothenic acid in regards to life span is outstanding. The increase in length of life is much greater than any experimental error and may be considered as a real contribution to the longevity of the fruit fly, and presumably is one of the factors in royal jelly that aids in prolonging the life of the queen bee.

Discussion

The role of pantothenic acid in human nutrition has not been determined. It is widely distributed in very small quantities in nature, and consequently a deficiency in humans has not been observed. The effects, if any, of an increased intake over a period of time have not been investigated. The cumulative effects of vitamins have been practically neglected, and pantothenic acid has received more than its share of neglect.

However some very interesting data have accumulated on the occurrence of panto-

Name	g/1000 g. Nutrient Med.	No. of flies	Average length of life in days	Prob. error of the mean	Percentage change over controls
Controls	——	99	13.3	±0.4	
Dehydrated Royal Jelly	0.33	57	13.3	±0.7	0.0
Royal Jelly	6.67	79	15.5	±0.5	16.5
Fraction X Ether Sol.	0.33	66	13.0	±0.6	−2.3
Fraction Y Ether Insol.	0.33	63	13.3	±0.6	0.0
Ether Insol.	6.67	50	13.4	±0.7	0.7
Fraction I–1 (Carbohydrates)	0.33	56	13.5	±0.7	1.5
Fraction I–2 (Water sol. protein)	0.33	62	13.4	±0.6	0.7
Fraction I–3 (Water insol. protein)	0.33	50	13.3	±0.6	0.0
Fraction S–1 (Phenols)	0.33	50	12.5	±0.5	−6.0
Fraction S–2, 3. (Water sol. and	0.33	69	13.4	±0.6	0.7
insol. acids)	6.67	53	14.5	±0.7	9.0
Fraction S–4 (Sterols, glycerides)	0.33	60	13.5	±0.6	1.5
Fraction S–5 (Wax)	0.33	51	13.0	±0.8	−2.3
Fraction S–6 (Phospholipids)	0.33	57	13.1	±0.7	−1.5
Calcium Pantothenate	0.5	98	17.0	±0.5	27.8

Figure 3.

thenic acid. The food especially designed for the growth of the young, human milk (6), is one of the best sources of pantothenic acid, 2.5 μ g/c.c., and colostrum (6) is even richer than milk, 3 μ g/c.c. Human placentas (31) contain large amounts of pantothenic acid, 20.8 μ g/g. dry basis. The ratio of the occurrence of some of the B vitamins in the human placenta is as follows, B_1, 29: B_2, 94: niacin, 1244; pantothenic acid, 170: biotin, 1.

Periodic fasting increases the life span of rats (4). Apparently a younger type of tissue is retained. Also a restricted caloric intake concentrates the B vitamins in the tissues of the rat (9) as well as increases the life span. Increases of 15 to 130 per cent of pantothenic acid were observed for various tissues on a restricted caloric intake (9).

One thing in common may be deduced from the investigations cited. Wherever young, actively growing tissue is present as in the placenta, food for young tissue as in milk or colostrum, or young tissue induced by a restricted caloric intake which results in an extension of the life span of rats (24, 32), then pantothenic acid is found in unusually high concentrations. Therefore, the evidence from other fields tends to bear out the view that pantothenic acid has some influence upon longevity as was found in the present investigation. In fact, a deficiency of pantothenic acid has been postulated as a cause of premature senescence in the rat (33), and this phenomenum may be the explanation of the premature senility changes on certain diets observed, and suggested, by Morgan (26).

Pantothenic acid is one of the least toxic of the B vitamins. Even one gram a day per kilogram of body weight was tolerated by dogs and monkeys (3). The requirements for humans are unknown but have been estimated as being about 11 to 15 mg. per day (11). Even this figure, which was based upon the prevention of an apparent deficiency, is not being met by an average American diet of 2500 calories (5). This study (5) showed that two-thirds to three-fourths of the population obtain only 4.9 mg. per 2500 calories. It has also been demonstrated (30) that pantothenic acid increases the reticulocytes as well as liver if ingested or injected at a level of 8 mg. per kg. body weight in rats. For a 70 kg. man this is the same level as found for 1000 gm. of nutrients in royal jelly.

The mechanism of the use of pantothenic acid in the body is unknown. Whether it acts as a longevity factor per se or as a limiting factor for the utilization of other vitamins has not been determined for humans. However for fruit flies it probably acts in both ways, as an anti-aging effect, and as a limiting factor with synergistic action for other vitamins as will be described in the second paper of this investigation (10).

Even the quantities of pantothenic acid to be used for cumulative testing on humans can only be estimated at about 100 mg. per day with an upper limit of 500 mg. per day. Such an estimate is based on the occurrence of pantothenic acid in very young tissue, and the upper limit as that found in royal jelly assuming it to be the sole food source for a life form, the queen bee. The latter assumption is not quite correct as the queen bee feeds on pollen, honey, nectars, bee-bread, etc., as well as royal jelly during the heavy laying seasons. Therefore, such an estimate for testing the cumulative effect of pantothenic acid may be considered as a first approximation only. Fortunately the nontoxicity of pantothenic acid permits the use of almost any reasonable amount. However, there is one thing that is evident, and that is that the role of pantothenic acid in human nutrition is probably more important than has been hitherto assumed.

Summary

1. Royal jelly was separated into fractions according to its chemical composition.

2. Royal jelly and its chemical components were investigated for longevity factors using Drosophila melanogaster as the test organism.

3. Raw, dehydrated royal jelly was found

to have beneficial effects on the life span of fruit flies.

4. Pantothenic acid was identified as the primary anti-aging factor in royal jelly.

5. Other chemical components of royal jelly have very little or, in some cases, slightly detrimental effects upon the life span of fruit flies.

6. The occurrence of pantothenic acid in young tissue, and in food especially designed for young, rapidly metabolizing tissue, was discussed in relation to the identification of pantothenic acid as the primary anti-aging factor in royal jelly.

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Submitted for publication September 20, 1947

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The Use of Drosophila Melanogaster as a Screening Agent for Longevity Factors.

II. The Effects of Biotin, Pyridoxine, Sodium Yeast Nucleate, and Pantothenic Acid on the Life Span of the Fruit Fly.

THOMAS S. GARDNER

IN EXPERIMENTS CONDUCTED WITH DROSOPHILA MELANOGASTER, DR. GARDNER NOTED THAT BIOTIN HAD NO EFFECT UPON THE LIFE SPAN, BUT BOTH PYRIDOXINE AND SODIUM YEAST NUCLEATE LENGTHENED IT. THESE THREE SUBSTANCES IN COMBINATION MATERIALLY EXTENDED THE SPAN OF LIFE, AND WITH THE ADDITION OF PANTOTHENIC ACID A SUBSTANTIAL INCREASE WAS DEMONSTRATED.

THE effects of the B-vitamins on longevity have not been investigated to any extent for any form of life. The therapeutic effects of the vitamins have received most attention but their cumulative effects have received scant notice. If a deficiency of a vitamin results in a serious or very apparent syndrome it has been carefully examined for therapeutic use. However, if a vitamin does not exhibit a deficiency in a relatively short time, especially in humans, the vitamin is apt to be neglected with the assumption that it is either not necessary for general well-being, or necessary only in small quantities. This is especially true if the vitamin is widely distributed in nature in small amounts. The effects, if any, of larger intakes than just necessary to prevent the appearance of deficiency syndromes, or any cumulative effects it may have are, therefore, ignored.

Deficiencies of thiamine (B_1), riboflavin (B_2), and nicotinic acid result in such serious syndromes if supplied in inadequate amounts that a great deal of attention has been given to them. On the other hand, pantothenic acid, pyridoxine, and biotin have received relatively only scant consideration. Serious deficiencies of the latter have seldom, if at all, been observed in man. The cumulative effects of increased intakes have not been investigated for any organism.

In the first paper of this series (5) it was demonstrated that pantothenic acid was a longevity factor for the fruit fly (D. melanogaster), and presumably for the honeybee. It was found that royal jelly increased the life span of fruit flies, and the essential ingredient for this effect was characterized as pantothenic acid.

It has been demonstrated that yeast nucleic acid increases the life span of white mice if fed from birth at a level of 25 mg. per day six days a week (10) and also if fed at a level of 2.5 mg. per day when the mice start receiving it at the 600 day level (4). The effect of yeast nucleic acid, or its soluble sodium salt, on fruit flies has not been investigated. Therefore, it was considered advantageous to extend the investigation on fruit flies carried out on royal jelly (5) which characterized pantothenic acid as the primary longevity factor, to include the B-vitamins, biotin and pyridoxine, and also sodium yeast nucleate. In recent years the synergistic action of nutrients has been emphasized. In order to check this phase, biotin, pyridoxin, and sodium yeast nucleate were investigated separately, in combination, and in combination with pantothenic acid.

EXPERIMENTAL

A hardy strain of fruit flies (Drosophila melanogaster oregon) was used in this in-

Dr. Thomas S. Gardner received his B.S. degree from the Tennessee State Teachers' College in 1931, his M.S. from the University of Tennessee in 1936, and his Ph.D. in organic chemistry from Ohio State University in 1941. He was a du Pont fellow at the Massachusetts Institute of Technology in 1941 and 1942, and a chemist with the Tennessee Eastman Corporation from 1942 until recently. At present he is with the scientific department of Hoffman-La Roche, Inc., in Nutley, New Jersey. His research has included work with carbohydrates, cellulose, and wood distillation products.

This paper was presented before the Division of Biological Chemistry at the New York meeting of the American Chemical Society in September, 1947.

Dr. M. H. Harnly, Department of Zoology, Washington Square, New York, New York, supplied the initial culture of D. melanogaster. Dr. Charles N. Frey of the Fleischmann Laboratories, New York, New York, supplied the sodium yeast nucleate, sample OA-588, 10-4-45.

vestigation. The medium consisted of Fleischmann Yeast in water with acetic acid as a sterilizing medium in addition to heat sterilization at 100 C. The preparation of the cultures was described in detail in the first paper (5). The water soluble vitamins and sodium yeast nucleate were added in solution in cold, sterile water to cold, previously sterilized culture mediums. This was done in order to prevent breakdown of samples containing pantothenic acid, which is not very stable to heat, and hot acid solutions. Extreme care was exercised to keep all cultures free of bacteria as the B-vitamins used are powerful promoters of bacterial growth which will destroy the cultures if allowed to get a start.

Fifty to 100 flies were used to ascertain each average life span, and only 10 to 15 flies were allowed in each bottle. The cultures were maintained at 30 C. as it has been shown (8) that the length of life of fruit flies is a function of temperature. The average length of life of the controls fell within the range found by Loeb and Northrop (8). Cultures for this investigation were run concurrently with the cultures for many of the previous investigations and consequently the average length of life of the controls was determined at one time.

Results

Figure 1 summarizes the average length of life obtained for all samples for the inclusion of the stated quantities of biotin, pyridoxine, sodium yeast nucleate, alone, in combination, and in combination with pantothenic acid. It will be observed that biotin has no effect on the fruit flies insofar as length of life is concerned. Pyridoxine gives an average increase of life of 10.5 per cent and sodium yeast nucleate, 11.3 per cent. However, when biotin, pyridoxine, and so-

Name	g/1000 g. Nutrient Med.	No. of flies	Average length of life in days	Prob. error of the mean	Percentage change over controls
Controls	——	99	13.3	±0.4	
Biotin	0.0067	56	13.3	±0.6	0.00
Sodium Yeast Nucleate	5.0	55	14.8	±0.7	11.3
Pyridoxine (B_6)	0.025	58	14.7	±0.7	10.5
First Comb:					
Biotin	0.0067				
Pyridoxine	0.025				
Sodium Yeast Nucleate	5.0	89	16.0	±0.6	20.3
Second Comb:					
First comb. plus Calcium Pantothenate	0.5	98	19.5	±0.5	46.6

Figure 1.

dium yeast nucleate are used to supplement one another the life span is increased by 20.3 per cent, which is lower than the increase obtained by the use of pantothenic acid alone, i.e., 27.8 per cent.

The addition of pantothenic acid to biotin, pyridoxine, and sodium yeast nucleate yields the surprising increase in life span of 46.6 per cent. It would appear that the various improvements exert a synergistic action upon each other to yield a very favorable increase in life span for the fruit fly, greater than for any tested nutrient taken alone. The favorable effect of pantothenic acid is significant because of its identification as a longevity factor in royal jelly (5).

Discussion

Biotin deficiency in man can only be induced with difficulty. A recent review (1) of the place of biotin in human nutrition indicates that insufficient work has been carried out to justify its use either therapeutically, or for its cumulative effects, if any. However, its failure to affect the life span of fruit flies cannot be considered a criteria of its effect on mammals.

Pyridoxine (B_6) has shown more promise than biotin in human nutrition. Several therapeutic uses are in the clinical testing stage, for example, its use in radiation sickness to build up leucocyte count (14). Its role in protein synthesis, enzymatic reactions, and possibly in fat metabolism has been discussed in several reviews (1, 2).

Several very significant investigations on pyridoxine have been carried out by Stoerk, Eisen, and John (16, 17). They found that rats deficient in pyridoxine failed to develop complementary bodies on immunization with washed sheep erythrocytes. The failure to develop adequate antibody levels on infection would usually be fatal to any life form requiring such a mechanism of defense. Therefore if there is any relationship between the mechanism of defense of the organism of fruit flies and mammals, the increased life spans obtained by pyridoxine would be easier to formulate into a suitable hypothesis. The importance of pyridoxine in human nutrition may be greater than has been realized and may await only properly designed experimental work on increased pyridoxine intake to yield satisfactory results that can be applied to human nutrition.

The increase of the life spans of fruit flies by sodium yeast nucleate is of especial interest because of the effect of yeast nucleic acid on the longevity of white mice (4, 10). Whether nucleic acids increase resistance as has been postulated (4) or are involved in cellular metabolism in nucleoprotein synthesis (10) to foster longer life spans has not been determined.

A deficiency of the B-vitamins seriously affects phagocytic activity (3) and greater activity was observed at increased levels of intake (3). Pyridoxine and pantothenic acid were found to be in this class, as well as thiamine, riboflavin, choline, and ascorbic acid. There is increasing evidence not only that the natural defenses of the body to internal breakdown are very closely connected with adequate nutritional intakes, but also that greatly increased intakes, or optimal nutrition according to the Sherman nomenclature (12) favor better resistance. Antibody-complementary reaction and phagocytic activity all make up one of the most potent barriers to infection, as well as general internal breakdown, that the organism possesses.

A great deal of evidence has been collected on the synergistic effect of nutrients upon one another. Recent reviews (11, 19) show that almost any function of the various vitamins may be blocked by appropriate chemical metabolites, and, which is just as important, the effect of any nutrient may not only be augmented but changed and enhanced in a beneficial manner by increased intake of other natural factors.

Deficient intakes of substances may then be considered as limiting factors in the sense that if they are ingested in deficient or maximal nutritional intakes, the organism may respond in a negative or positive manner. An excellent example of positive effects of sub-

stances ingested is the enhanced effect of vitamin C with the vitamin P active substances (7, 18). A negative effect is the increased susceptibility to pneumococcal infection of mice ingesting whole wheat bread as compared to white bread (6). Some factor in the whole wheat decreases the resistance of the mice. It is possible that future nutritional research will deal to a major extent with uncovering the problems of synergistic effects of the various nutrients upon one another.

The beneficial effect of pantothenic acid on fruit flies in increasing their life span (5), and the much greater effect on their longevity already enhanced by pyridoxine, sodium yeast nucleate, and perhaps biotin, suggests that it is a limiting factor. If so, its value would be difficult to determine unless it were used in large quantities, in addition to high intakes of the other vitamins. Fortunately pantothenic acid is one of the least toxic vitamins known. For example of its application, it has been demonstrated (9, 13) that Vitamin A increases the average life span of rats. Also work on the other vitamins indicate beneficial results which will not be enumerated here.

However, it has been recently shown that rats fed a natural diet corresponding to that of the major portion of the Northeastern United States, with vitamin supplements, showed no increase in the average life span (15). An examination of the vitamin supplements used discloses that only a fraction of pantothenic acid was used as compared to the values previously indicated for nutrition in another life form (5). Thus, it may be possible that a limiting factor in the investigation cited is pantothenic acid, or even some other uninvestigated vitamin or combination of vitamins. If such is the case, the anomalous results obtained (15) would be explainable.

The evidence that pantothenic acid is a limiting factor for longevity purposes is certainly not conclusive, but it is suggestive of that possibility. Further investigations on high intakes of pyridoxine and pantothenic acid should be fruitful for the aging problem. Yeast nucleic acid has already been shown to be a promising lead (4, 10).

This investigation and a preceding one (5) indicate that fruit flies under careful, bacteria free, and controlled conditions may be used to separate compounds having potential use for mammalian aging research. Whether or not similar results can be carried over into mammals has not been proved, although the fact that yeast nucleic acid is beneficial for both mice (4, 10) and fruit flies in lengthening the life span is very encouraging.

Summary

1. The effects of high supplements of biotin, pyridoxine, and sodium yeast nucleate used separately, in combination, and in combination with calcium pantothenate on the life spans of Drosophila melanogaster were investigated.

2. It was found that biotin had no effect upon the life span in the quantities used, but both pyridoxine and sodium yeast nucleate increased the life spans approximately 10 per cent each.

3. High intakes of biotin, pyridoxine, and sodium yeast nucleate in combination materially increased the life span (20.3 per cent) of fruit flies.

4. The addition of pantothenic acid as calcium pantothenate to the combination in (3) yielded a very great increase (46.6 per cent) in the life span of fruit flies.

5. In the discussion of these results some evidence was presented to indicate that pantothenic acid acted as a limiting factor for the utilization of the B-vitamins. Therefore increased pantothenic acid intake may enhance the beneficial effects of other nutrients.

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Submitted for publication September 20, 1947

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WHO IS OLD?

Death Rate in a Japanese Concentration Camp as a Criterion of Age

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ANALYZING THE POPULATION AND DEATH RATE FIGURES OF A JAPANESE CONCENTRATION CAMP, DR. BERGMAN FOUND THAT AGE WAS A DEFINITE FACTOR IN DETERMINING SURVIVAL OR DEATH OF THE PRISONERS.

EVERY prisoner in the Japanese concentration camps in Java saw the number of deaths rise by the day in the third year of the internment. Dominant was the impression that the older people paid an improportionately heavy toll. Here one said, "I still have a chance, I am not yet fifty;" there one heard, "I have not much chance left, I am fifty already." Or it was "If this is going on for another half year there will be no need to deliver us. It is not only the old people, but we will all be finished by then, liquidated."

However, it was evident also that age alone was not the discriminating factor. The previous life history too was very important. One of my patients, a pensioned soldier of about 47 years, came to the surgeon for a minor operation. The patient was thin, grey, and so weak he had some difficulty in coming up the doorsteps. He excused himself saying, "Sorry to keep you waiting, but I am not young any more, not by a long way, already 47 and 25 of them in the tropics!" The surgeon smiled at me across the table; he was 57 himself, thin also and weak from hunger, but still working. He also had more than 25 years in the tropics, but up to the internment had kept to another modus vivendi. But these are of course only examples, demonstrative, but not representative for the whole group of prisoners.

Is it then true that just simply getting older increases the chances of death in a camp, so much that there is a threshold between normal risk and almost certain ruin?

Perhaps an analysis of the population and death rate figures can be of value in trying to answer this question.

The camp history is briefly as follows. At the end of February, 1944, 10,350 male civilians between 10 and 85 years of age, coming from smaller camps throughout Java, were concentrated in a complex of empty military barracks, Camp IV, Tjimahi. Afterwards there were only few mutations, and only three of these really affected the death rate.* In March, 1944, there was a sharp rise in dysentery cases and subsequent death. Japanese headquarters in Batavia sent an order that nobody was to be allowed to die in the camp. This could not be prevented by force, so the very ill prisoners were sent to a nearby camp-hospital, from where only a few returned. The death rate in the camp itself fell, of course. In December, 1944, a group of about 500 sick and weak people was sent to camps in Middle Java. In May, 1945, another group of 760 similar cases were sent to Batavia. Of both these groups nearly three-fourths died, but they are not mentioned in the death list of Camp IV, Tjimahi.

The conditions of life were virtually the same for all prisoners. Not even one in two

* For completeness the other mutations are listed here. In October, 1944, a group of 1500 "dangerous" men, chiefs of business enterprises, civil servants of higher rank, ministers of various religions, university people, nobility, free masons, and Jews, were transported to Camp Baros. At the same time this group was replaced by a similar one from Batavia and Bandoeng. In April, 1945, a group of 66 Eurasian collaborators with the Japs were released. In May, 1945, about 600 "valid" people were sent to work on a railroad in Tjtjalenka, near Tjimahi. In the same month another 40 "dangerous" men were sent to Baros also near Tjimahi. These mutations did not affect the death rate of Camp IV seriously.

Dr. Bergman received his M.D. degree from the University of Utrecht in 1927. After serving as assistant in the Departments of Anatomy in Amsterdam and in Batavia, he became head of the Department of Anatomy of the medical school in Sourabaia. During his internment Dr. Bergman practiced general medicine in the camps Kesilir, Tangerang, Tjimahi IV, and Tjimahi-Baros. He became head of the medical department of the Netherlands-Indies Welfare organization for evacués in Victoria, Melbourne, Australia, in 1946, and in 1947 professor of anatomy and microscopic anatomy at the University of Indonesia, Batavia.

had been able to carry a small mattress or a pillow, or had found a couple of planks to lie down upon. Very few (a couple of hundred) had a camp stretcher. The majority had bare stones. It was very crowded; in the "best" quarters there was a square 2.25 m. long and 75 cm. wide. Quite often the available width was only 63 cm. After some months men of sixty years and older were put together in empty houses with some younger people to do the "corvee" work. In the whole camp there was much dysentery, avitaminosis, intestinal trouble, oedema, and the chances of infection were identical for all age groups.

Hunger was also the same for all groups. A few hundred prisoners, working in the kitchen or in the field outside the camp, could sometimes supplement their meager rations. At the very highest estimate, they managed with hard manual labor to reach 2000 calories a day. The rest had a ration between 1000 and 1250 calories a day.

The number of deaths recorded for Tjimahi IV is 744, from February, 1944, until August, 1945, out of 10,350 men, or a death rate of 48 pro mille per year. This is only about three times the normal death rate and at first sight it does not seem very high for a Japanese concentration camp. However for 1944 and 1945 separately, the death rates are 31.1 and 74.5 pro mille per year, which is a very pronounced difference. It already marks the weight of the time factor in the fate of the prisoners.

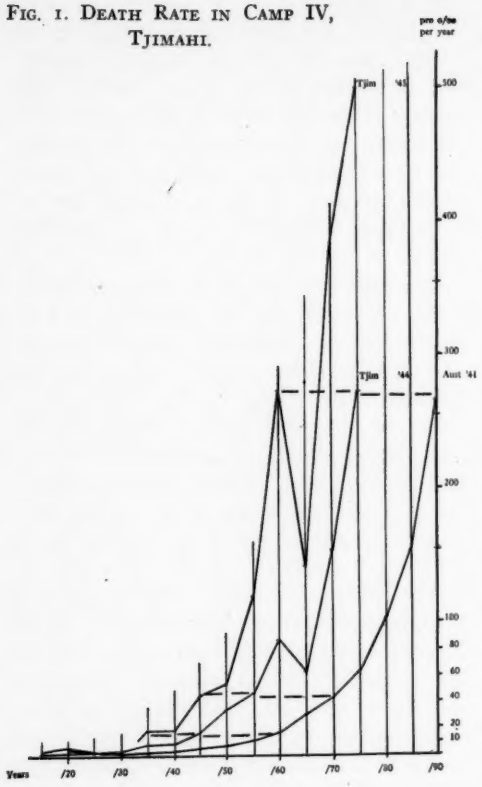
In table 1 are listed the death figures recorded in the different age groups per month. The higher figures are to be found in the columns of the 50- and 60-year groups. This is not conclusive because these groups were also numerically the highest in the camp population, most people of military age being interned in other camps as prisoners of war.

The number of people in each age group in March, 1944, and in January, 1945, is given in table 2, together with the number of deaths in these groups during the ten months of 1944 and the eight months of 1945. To make direct comparison possible, the year pro mille's are given with those for Australia in 1941. With the exception of the 16 to 20 year group where the figure is twice that for Australia, the figures up to the 35 year group are of the same order. At 35 the death rate rises suddenly and will continue to do so for the duration of the internment. At the same time the curves for 1944 and 1945 (Fig. 1) tend to diverge, not only from those for Australia, but also between themselves. The break in the curves shown at the 65 year group is influenced, as table 1 will show, by a seasonal factor—the lowering of dysentery morbidity accentuated perhaps in 1944 by the relative isolation in separate houses and in 1945 by the transportation of old people to Batavia.

In comparing the curves, we find a similar death rate —18 o/oo for the people of 60 years in Australia, 45 in Tjimahi, first period, and 35 in Tjimahi, second period. The same holds for the group of those 70 years in Australia —43 o/oo—, 55 years in Tjimahi, first period, and 45 in Tjimahi, second period. And also —270 o/oo— for the 90-year group in Australia, the 75 group in Tjimahi, first period, and the 60 year group in Tjimahi, second period.

Put in another way, this means that there is a difference of 15 years of age between people living in a civilized society and a similar group after two and one-half years in a Japanese camp, which after another eight months of camp life increases to 25 years.

FIG. 1. DEATH RATE IN CAMP IV, TJIMAHI.



The harm done to the individuals in this case manifests itself in the increased death rate and can be put down to a process of rapid pathologic aging.

Of course the death rate is not the only indication of this process; there are many more, but the others are, although clearly visible, difficult to take down in figures. The premature greying of the hair, the excessive wrinkling of the skin first caused by the disappearance of the subcutaneous fat and later by the loss of elasticity, the difficulty in walking, even when there was no other sign of beri-beri, the general hypotony of the musculature, the monotony in thought, the difficulty experienced in realizing and analyzing present problems, the predominance of past memories—all these and many more signs pointed in the same direction. But as mentioned before, the death rate as a symptom has two definite advantages, it is calculable and it is irreversible.

The process itself is fortunately not irreversible. Every physician with experience among ex-prisoners knows that many of them made remarkable recoveries. They regained their physical ability and mental fit-

TABLE 1. NUMBER OF DEATHS PER MONTH AND AGE PER GROUP IN CAMP IV, TJIMAHI

1944	11-15	16-20	21-25	26-30	31-35	36-40	41-45	46-50	51-55	56-60	61-65	66-70	71-75	76-80	80-85	Total
March					1	1	2	4	3	7	5	1				24
April			1	1		2	2	9	15	25	3	3	2	1		64
May						1	3	2	11	5	6	2	1			31
June							1	1	6	3	3	1			1	16
July		1			1			4	6	5		1				18
August		1					1	2	3	3		1	1			12
September					1		1		2	2						6
October		2			1	1	1	3	7	6						21
November							1	4	8	11	5	3	3			35
December					1	1	3	5	4	16	4	4	3			41
1945																
January		1				1	3	8	16	23	5	2	1	1		60
February					1	4	5	6	10	23	7	3	1	1		61
March		1			3		3	8	13	31	8	2				69
April	1					1	3	5	21	32	8	5	5			81
May		1	1		1	2	8	5	25	39	9	6		1		98
June					1	2	4	2	11	12	1	4			1	38
July					1		1	2	10	15	1	1				31
August		1			1		4	3	13	13	2	1				38
To'al	1	8	2	1	13	16	45	73	184	271	67	40	17	4	2	744

TABLE 2. DEATH RATE IN CAMP IV, TJIMAHI

Age-groups	Number of persons				Pro mille per year Tjimahi		Austr.
	Alive Mar. '44	Dead in '44	Alive Jan. '45	Dead in '45	1944	1945	1941
11-15	406	—	405	1	—	2.7	1.07
16-20	1320	4	1296	4	3.6	5.0	1.57
21-25	675	1	656	1	1.8	2.3	2.04
26-30	525	1	499	—	2.3	—	1.98
31-35	709	5	673	8	8.5	18.2	2.31
36-40	900	6	845	10	8.0	17.8	3.43
41-45	1094	15	1036	30	16.4	43.5	4.56
46-50	1177	34	1100	39	34.7	53.0	7.36
51-55	1640	65	1485	119	47.5	120.	11.53
56-60	1215	83	1028	188	82.0	275.	17.93
61-65	499	26	437	41	62.5	141.	29.79
66-70	126	16	94	24	152.	383.	43.22
71-75	44	10	21	7	272.	500.	64.27
76-80	17	1	12	3	71.	375.	104.6
81-85	3	1	2	1	400.	750.	154.6
85-90							264.8

ness to an astonishing degree; most of them are at work again, although they remain more grey and wrinkled than fiits their real age.

Of course a certain number, it is difficult to guess how many, did not recover completely and died in the year following the victory; some recovered partially and remained at the pathologic age level already reached.

As for the question how long life in such conditions can be prolonged, there can only be very crude guesswork. But certainly the generally accepted view was quite sombre. If death progression had gone on at the same rate as in the last eight months, it would have taken another eight months to kill a quarter of the prisoners above 30, and another half year to reduce their number by half, whereby indeed the age groups above 50 would practically have been eliminated.

SUMMARY

The number of deaths per month and per age group and the death rate in Camp IV, Tjimahi, have been analyzed. It is concluded that while age was not the only factor involved in the number of deaths, after the age of 35 the death rate rose suddenly and continued to do so for the duration of the internment.

Submitted for publication September 20, 1947

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Maturity and Ageing. A Course in the Institute of Child Welfare of the University of Minnesota

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THE NEED TO PREPARE STUDENTS TO WORK WITH PENSIONERS AND ELDERLY CLIENTS AS WELL AS WITH PARENTS HAS CRYSTALLIZED IN A COURSE AT THE UNIVERSITY OF MINNESOTA. THE COURSE IS ALSO DESIGNED TO ENABLE THE STUDENT TO ANTICIPATE AND UNDERSTAND THE VARIOUS CHANGES IN HIMSELF WHICH COME WITH INCREASING YEARS.

ON FIRST thought, a course in maturity and aging may seem a bit incongruous in the offerings of an Institute of Child Welfare. However, the need for such a course had been apparent for some years at the University of Minnesota, and "Maturity and Aging: Developmental Changes and Adjustment" was first listed among the offerings of the Institute of Child Welfare for the year 1945.

As frequently happens, the course appearing in 1945 had had its precursors. When the General College was first begun at the University in 1933, with emphasis on a practical general education, a course was instituted there called "Human Development." This course, taught for many years by Professor John E. Anderson, Director of the Institute of Child Welfare, and later by other members of the Institute staff, covered the problems of human psychology from a developmental viewpoint, taking the individual from birth into the years of later maturity. Not much emphasis was given to the last years of the life span, but considerable emphasis was given to the developmental changes in later adolescence, early adulthood and middle life. The purpose of this course was based on the belief that a well-rounded general education should prepare young people to assume their responsibilities as adults and to assist them in the adjustments that would lie ahead of them in the years after their separation from the University.

From a theoretical point of view, a course on maturity seemed worth organizing in the Institute of Child Welfare curriculum. The Institute has courses describing the young child, the older child, and the adolescent. It seemed that there was enough research and writing available to organize a worth-while course at the senior and graduate level on maturity and the aging process, to round out the developmental span. After all, any segment of this span is an arbitrary division; it is generally recognized that the developmental process is a unity, and that within this process various parts and systems have their own periods of growth and decline.

There were practical reasons, also, for instituting such a course. Since its inception, the Institute of Child Welfare has made a positive contribution in the area of parent education. Students preparing for professional work with parents have needed some understanding of the psychology of the adult, particularly as that psychology changes. The adult's relationship to children in childhood, adolescence, and young adulthood changes not only because of children's growth through these periods, but also because of the adult's changing adjustments to his environment. Many of the young people training for work with parents are themselves young and need some points of view concerning likely changes in the individual during the years of maturity.

There have been requests from other departments for a descriptive course of the later years of maturity. Students planning to work with pensioners, elderly clients, and the like have needed a systematic under-

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standing of the aging process to help them make adjustments to their clients and to assist in formulating philosophies of relationship and treatment with older clients.

The course to be described here was first placed in the catalog as a Readings course for the year 1945–46. In the year 1946–47 it was made a lecture course and open to qualified seniors and graduate students. During the year 1947–48, a section of this course will be offered in the General Extension Division. It is hoped that a group of older persons may take the Extension course primarily to acquaint themselves with the meanings of the changes they themselves are experiencing. Here it may have a more practical interpretive or therapeutic significance than a theoretic or orientation significance. This section of the course is being offered experimentally and will be followed with considerable interest by this department.

In the hope that other schools will become interested in doing instruction and research in this important area of human experience, we are presenting the outline of the course as it has been developed during the past academic year for whatever worth it may be to readers. There are few precedents for the organization of such material, and it has been convenient to cast this course into much the same form as other developmental courses. The lectures and discussions are organized under the following several heads:

1. General problems of maturity and aging; demographic aspects of aging.
2. The biology of aging.
3. Changes in social relationships during maturity and old age.
4. Changes in interests and attitudes.
5. Personality and temperament in maturity and senescence.
6. Intellectual developments in maturity and the later years.
7. Occupational and professional achievements of older persons.
8. The older person in the family.
9. The older person in a changing society.
10. Anthropologic approaches to problems of aging.

In the actual presentation of materials, considerably more time has been spent on topics 1 through 6, with less attention being given problems 7, 8, and 9, and a very brief consideration given to 10. It is believed that the first topics are more fundamental in terms of basic materials in a psychologically oriented course, although some attention should be given to the occupational and professional achievements of individuals at the different age levels through maturity, some of the vocational problems faced by the older worker, the older persons in the family, and the implications of changing social demands for the older person.

The procedure was based primarily on lectures, with the person in charge occasionally calling on a campus expert to present some phases of technical subjects, such as the biology of aging, medical problems in older ages, mental deterioration in the senile psychoses, and the like. There were a number of discussions participated in by members of the class, reviewing the lecture material. Since the class was relatively small, it was possible to have these discussions centered about a seminar table.

The literature for the course was placed on a reserve shelf in the University library. Members read a series of general assignments and then did more specialized reading, which was reported in the form of a term paper, with bibliography. The general readings covered by all students were selected from the following sources:

Cowdry, E. V.: *Problems of Aging* (Rev.), Williams and Wilkins, Baltimore, 1942, 936 pages (most of the text).

Goodenough, Florence L.: *Developmental Psychology* (Rev. ed.) D. Appleton-Century, New York, 1945. (Appropriate sections.)

Lawton, George.: *New Goals for Old Age.* Columbia University Press, New York, 1944, 210 pages.

Pressey, S. L., Janney, J. E., and Kuhlen, R. G.: *Life: A Psychological Survey.* Harpers, New York, 1939, 654 pages (chapters 2 through 11).

Simmons, Leo W.: *The Role of the Aged in Primitive Society.* Yale University Press, New Haven, 1945, 317 pages.

Thorndike, E. L.: *Human Nature and the Social Order.* Macmillan, New York, 1940, (a number of chapters).

More specialized reading was done in psychologic, sociologic, and medical journals, and in a few additional books addressed specifically to problems of aging.

In addition to these assignments, each student wrote a paper, according to the following instructions:

Write an autobiography of your own life, taking the position of a person past the age of sixty. In terms of your present interests, abilities, skills, knowledges, and your probable vocational career, give an account of your own later maturity, bringing out any physical conditions you may likely develop, the course of your intellectual, social, and emotional life, and your expected provisions for a creative old age. Apply in every way possible the specific knowledges and insights gained from your readings and study.

The students reported this assignment, though difficult, to be one of the most interesting problems they had met in their school experience. The majority commented that it required them to organize and interpret their readings and notes in a manner both new and meaningful to them.

Summary

At the University of Minnesota, the Institute of Child Welfare has established a course on developmental changes during maturity and old age to complete its cycle of basic instruction concerning the child, adolescent, and adult. Students preparing for vocational counselling, parent education, social work, clinical psychology, and other professional fields find in this course a summary of current knowledge about the adult and the adjustmental problems brought by advancing years. Anticipating the increased numbers of older adults in society, it is hoped that other institutions may see fit to organize instruction and to encourage research in this important area.

Submitted for publication November 14, 1947

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The Effects Of Progesterone, Oestradiol, Thyroid Hormone, and Androsterone on the Artificial Premature "Climacteric" of Pure Gonadal Origin Produced by Ovariectomy in Rats

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IN THE LAST OF A SERIES OF FOUR PAPERS DR. KORENCHEVSKY AND DR. JONES REPORT ON THE EFFECTS OF PLURIHORMONAL TREATMENT ON BODY WEIGHT AND FAT DEPOSITION; UTERUS, VAGINA, LIVER, KIDNEYS, ADRENALS, THYROID; WEIGHTS OF PREPUTIAL GLANDS, HYPOPHYSIS, THYMUS, SPLEEN, HEART OF OVARIECTOMISED RATS, AND CONCLUDE THAT IN A LIMITED SENSE PLURIHORMAL TREATMENT NOT ONLY ARRESTS THE AGING INVOLUTION OF SOME ORGANS, BUT ALSO IS ABLE TO RETURN THEIR RELATIVE WEIGHTS AND APPARENTLY THEIR HISTOLOGIC STRUCTURE TO A LEVEL OBSERVED AT A YOUNGER AGE.

IN OUR previous papers (9, 18, 19) the effects of androgenic, oestrogenic, and thyroid hormones were studied on weight and histology of organs in rats in which a premature artificial climacteric had been produced by ovariectomy. In the present paper the effects of progesterone were investigated in combination with oestradiol, androsterone, and thyroid hormone. Thus, this paper concludes our scheme on the action of the main sex hormones naturally present in the female organism.

It is obvious, however, that our experiments were limited by the technique used. Therefore they can give only a very limited answer to the major question approached by our investigation, namely, whether the hormones used have or have not true anti-aging properties. A complete understanding and accurate definition of the anti-aging properties of any factor examined could be obtained only after the performance of several morphologic, physiologic, and biochemical investigations, both experimental and clinical. Such investigations should be carried out both on aging and old individuals, normal individuals, and those with deficiencies in function of the main organs.

As in our previous papers, the literature will be limited to investigations made on ovariectomised rats. Courrier (5) in his excellent book has made a comprehensive review of the literature, including his own numerous papers, on the effects of progesterone and on the changes in organs during pregnancy.

METHODS

Three experiments were performed on a total of 78 ovariectomised rats, 14 control rats and 64 rats treated with the hormones in different combinations. The arrangement of the experiments into different groups, the weights of organs, and the doses of the hormones used are given in tables 1 to 3.

Since experiments I and II were of the same duration and they have been performed on rats of the same age and treated with the same doses of the hormones, in table 2 the relative weights of their organs were pooled. The final average age of rats in the first two experiments was 190 days and the duration of the experiment was 52 days; the respective data in the experiment III were 175 and 43 days.

For the reasons detailed in our previous

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Dr. Vera Jones obtained her B.Sc. degree in zoology in 1941 and her Ph.D. degree in 1944 at Liverpool University. She has been a research worker at Liverpool University and at Reading University, National Institute for Research in Dairying. Since January, 1945, she has been with the Gerontological Research Unit at Oxford University. Her work has been chiefly with cancer research and gerontology.

Mr. B. Benjamin, Head of the Statistical Bureau of the London County Council, made the greater part of the statistical analyses.

paper (18, p. 325), the relative weights of organs per unit of fat-free bodyweight are of main importance. Therefore in tables 2 and 3 these values are given.

In order, however, to show that the changes in actual weights were of the same character and similar significance, the actual weights of organs in experiment I (as example) were also statistically analyzed and the results are given in table 1.

For measurement of size of cells and of zones of adrenals the method of weighing paper replicas was used. This has been described in our previous papers (9, 19). Details of the measurement of nuclei and definition of large cells and large nuclei were also given in our previous paper (9, p. 337). One of us (V. E. Jones) has made an attempt to estimate the number of cells in the fasciculata zone of adrenals by dividing the average weight of paper replica of this zone by the average weight of the paper replica of the fasciculata cell (after reducing the weight of replicas to the same magnification, since the zones were outlined at magn. × 48 and the cells at × 720). The results are given in column 7 of table 7.

It must however be emphasized that this method can give only a very rough estimation, since it does not take into consideration the variation in size of spaces occupied by blood vessels and corrects only approximately the variation in size of the fasciculata cells, which gradually decrease in size from the outer part of the fasciculata zone towards the reticularis zone. With the aim of correcting the latter error, paper replicas were outlined only from cells in the median part of the zone, since it was presumed that these represented an average size of fasciculata cell.

In the previous papers (9, 19) the method of paper replicas was used for estimation of the size of the cells and nuclei of the liver and kidney and of the adrenal zones after administration of androsterone, oestradiol, and thyroid hormone separately or in various combinations. Therefore since these estimations have already been done for these hormones and since the method is difficult and consumes much time, in the present paper it has been used in a part of the experiments only so as to show the effects of progesterone in the combinations used. In the other part of the experiments the changes in size of cells and nuclei were judged approximately by comparing photomicrographs of the respective organs.

The administration of progesterone in the first two experiments was made in oily solution. In experiment III both progesterone and androsterone were injected in the form of an emulsion of crystals in 5 per cent gum acacia. In all experiments the same compound of oestradiol benzoate butyrate in oily solution was given as that used in our previous investigations. The advantages of

injecting crystalline suspensions of hormones and the best technique for this method have been described by Miescher, Gasche, and Frey (24). Desiccated thyroid was administered orally by pipette in the form of an emulsion. Statistical analyses were made using Fisher's "t" test for small samples. The histologic technique was the same as that used in our previous papers (9, 19). All photomicrographs were made from organs of the rats in Experiment III.

Effects on Body Weight and Fat Deposition

In the previous papers the literature was reviewed, and the results of our own experiments were given on the effects of gonadectomy and of androsterone, oestradiol (18), and thyroid hormone (17, 18) on body weight and fat deposition in female rats.

Similar results have been obtained in the present experiments—slight gain in bodyweight and fat deposition after androsterone injections, and a decrease in these values after thyroid hormone and oestradiol administration. After combined injections, with the doses used, androsterone and progesterone did not improve significantly the depressing effect of the other two hormones. In the experiments by Hart and Cole (7) rats, which had pregnancies or were carried through pseudopregnancy, grew better. Bogart, Lasley, and Mayer (2) found that not only pregnancy and pseudopregnancy, but progesterone as well accelerated the growth of rats. Progesterone, however, was unable to prevent significantly the depressing effect of oestradiol on growth. The fat and water content in the carcasses of rats given progesterone did not show any change as compared with control rats.

Effects on Uterus

In previous papers (18, 19) the changes obtained both in weight and histologic structure of the uterus, after administration of oestradiol B.B., androsterone, and thyroid hormone, administered separately or in combination, were described. The literature on the subject has also been reviewed.

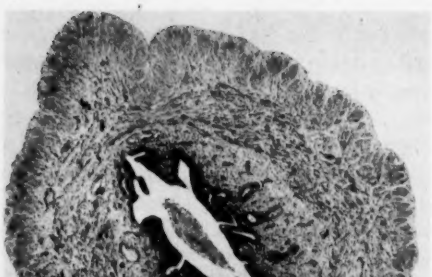
In the present experiments the results previously obtained with these hormones were confirmed and therefore will not be described again. An increased weight of uterus after injections of androsterone (table 3) was statistically not significant. The progestational changes in the uterus obtained after combined administration of oestradiol and described in the rat by several authors (for progesterone are well known and have been example, 5, 12, 13, 14).

Hisaw, Greep, and Fevold (8) obtained in ovariectomized monkeys and rabbits preprogestational or progestational changes after injection of progesterone alone. In ovariectomised rats these injections produced a slight enlargement of the atrophic uterus in which the epithelium showed an increase in thickness with occasional mitoses. Selye (26) claimed that progesterone alone causes typical progestational changes in the uterus of spayed rats.

In the present experiments there was a difference between the changes obtained in the experiments I and II (oily solution of progesterone injected during the last nineteen days of the experiment only) as compared with experiment III (emulsion of crystals of progesterone injected during the whole experiment). In the first case the progestational changes were weak and the epithelium remained high, i.e., being of the typical oestrogenic type. In experiment III the progestational changes were more pronounced, but the foldings of the mucosa were much less developed (fig. 1) than in the uteri of rats which had received androsterone and thyroid in addition to oestradiol and progesterone (fig. 2).

Thus it appears that for the best development of progestational changes in the uterus all four hormones used are necessary.

As before (13, 14) metaplastic changes of varying degree were present in the uterine epithelium and glands of all of the 8 rats into which oestradiol alone was injected. On the contrary, in all of the 21 rats into which, besides oestradiol, progesterone was also injected alone or in combination with andros-



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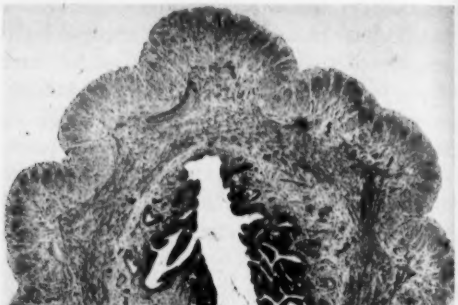

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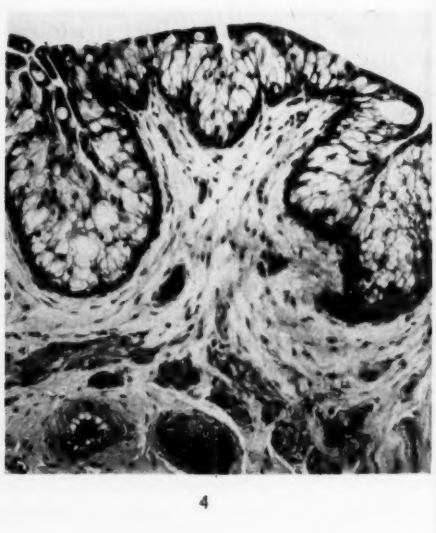

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HORN OF UTERUS (X38) AND VAGINA (X120), transverse sections
Haematoxylin + Eosin.

FIG. 1. Rat injected with progesterone and oestradiol B.B. Progestational foldings of mucosa slightly developed. Uterus 286 mg.

FIG. 2. Rat receiving progesterone, oestradiol B.B., androsterone and dessicated thyroid. Typical well developed lace-like folding of mucosa. Uterus 333 mg.

FIG. 3. Rat the same as in fig. 1. Typical well developed progestational mucification of vaginal epithelium. Vagina 391 mg.

FIG. 4. Rat from the same group as in fig. 2. Fewer rows of mucified vaginal epithelium than in fig. 3. Vagina 466 mg.

terone and thyroid hormone, these metaplastic changes were absent. In the previous experiments (12, 13, 14, 19) androsterone or thyroid hormone could not prevent the development of oestrogenic metaplastic changes in the epithelium. In the present experiments they were also present in the group of rats treated simultaneously with oestradiol and thyroid hormone, although they occurred less frequently than in the group of rats injected with oestradiol alone. It is also necessary to emphasize that progesterone is able to prevent adenoma-like formations in uteri of rats injected with oestradiol and androgenic hormones (14), and abdominal fibroid tumours caused by oestrogen administration (20, 21, 22).

Effects on Vagina

In our previous papers (18, 19) the changes obtained in weight and histology of the vagina after administration of androsterone, thyroid hormone, and oestradiol, separately or in combination, have been described, and the literature on the subject reviewed. The same results were obtained in the present paper. A statistically significant increase in weight of the vagina was obtained after administration of adrosterone ($P< .001$) and thyroid ($P< .01$) in experiment III. In all oestradiol-injected groups an addition of any of the hormones used, separately or in combination, did not change the oestradiol weight of the vagina.

It is well known that administration of progesterone to ovariectomised rats previously treated with oestradiol produces mucification of the vaginal epithelium, which is a typical progestational change. It was considerably greater in experiment III than in experiments I and II. Therefore the administration of emulsified crystals of progesterone was more effective, both in the case of uterus and vagina, than injections of oily solution. The total dose of progesterone in experiment III (50 mg.), however, was greater than in experiments I and II (38 mg.).

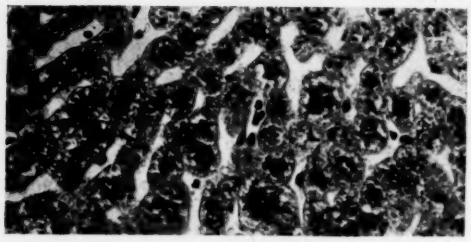
In contrast to the uterine changes, in the vagina the greatest degree of mucification was observed in rats injected only with progesterone and oestradiol (fig. 3) and not in those to which all four hormones were administered (fig. 4). This result was unexpected since both androsterone and thyroid tend to produce slight mucification of vaginal epithelium, as we observed in previous (19) and in the present experiments.

Effects on Liver

The effects on the liver of those doses and hormones which have been used in our present experiments (9) were confirmed in our present investigation.

Thus, the small doses used of thyroid hormone and oestradiol B.B., when administered separately, did not produce statistically significant changes in weight of the liver, but a significant increase ($P< .01$, table 2) was recorded after their simultaneous administration.

Histologically it was found (table 4) that after thyroid hormone administration there was a typically increased number of large nuclei ($P< .02$), or large cells ($P< .02$) and nuclei ($P< .01$) after oestradiol injections, and of all these values ($P< .05$-$.01$) after simultaneous administration of these two hormones. The cooperative effects were also seen in the number of mitoses (all three experiments were pooled for these counts): in control and rats injected with oestradiol —no mitoses, in the group injected with thyroid—0.2, and in the oestradiol + thyroid injected group—3.0 mitoses in a standard area (table 4). The same similarity to our previous results was found in the case of the *androsterone* effect: increased weight of liver ($P< .001$, table 3), larger cells (fig. 6), but no mitoses. The cytoplasm was lighter, with well defined basophilic granules more or less evenly distributed in the cytoplasm (fig. 6), while in the control rats these granules are packed mostly around the nucleus (fig. 5). Because of this, the nuclei of control rats appear on a photomicrograph to be angular and considerably larger than they actually are.



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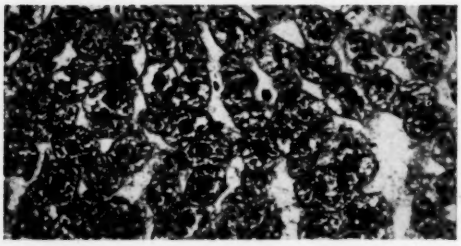

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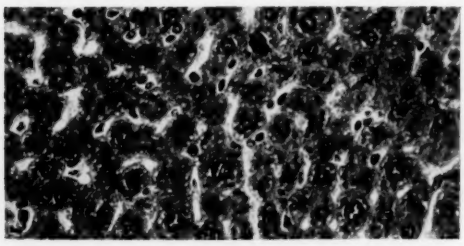

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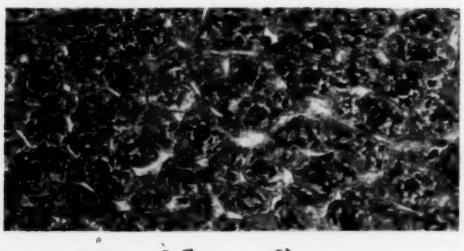

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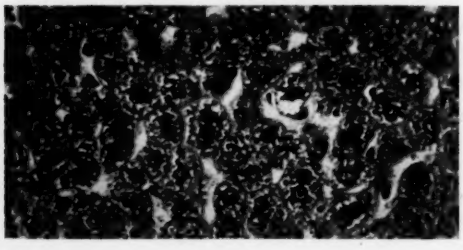


When injected with oestradiol, progesterone hypertrophied the liver ($P < .05$, tables 1 and 2)—especially with the larger dose ($P < .001$, table 3), increased the size of the liver cells ($P < .01$, table 4) and of the number of large nuclei ($P < .01$). Basophilic granules (fig. 8) were dispersed in the cytoplasm like those in livers of rats injected with androsterone, but they were not so sharply outlined as in the control or rats injected with androsterone. No mitoses were found in the livers of this group.

When thyroid hormone, alone or with androsterone, is administered simultaneously with progesterone and oestradiol, the liver undergoes considerable hypertrophy ($P < .01$-$.001$, tables 1, 2 and 3) as shown both by actual and relative weights. Histologically (table 4) in the liver of these rats all the measured values were increased: average size of the cells ($P < .05$), number of large cells ($P < .05$), and of large nuclei ($P < .02$). As compared with other groups, the number of mitoses (5.0 to 6.0 in a standard area) was the largest in these two groups. The basophilic granulation and demarcation between individual cells (fig. 9) were considerably better defined and the

LIVER, Haematoxylin + Eosin × 310.

FIG. 5. Control rat. Liver cells with sharply stained basophilic granules, packed chiefly around the nuclei, which, because of this, appear angular and larger than they actually are. Liver 5.85 gm.

FIG. 6. Rat injected with androsterone. The cells are larger than in fig. 5, with a lighter cytoplasm and dispersed but sharply stained basophilic granules. Liver 7.52 gm.

FIG. 7. Rat receiving desiccated thyroid. As compared with figs. 5 and 6, there is more solid and less vacualated darker cytoplasm, less defined basophilic granulation, increased number of large nuclei. Liver 7.53 gm.

FIG. 8. Rat injected with progesterone oestradiol B.B. Larger cells, hazy cytoplasm with dispersed, but less defined basophylic granules than in figs. 5 and 6. Liver 7.84 gm.

FIG. 9. Rat receiving all four hormones—progesterone, oestradiol B.B., androsterone, and desiccated thyroid. Cells similar to those in control rat, but with increased number of larger cells and nuclei. Dispersed well defined granules. Liver 7.87 gm.

bluish tint of cytoplasm was much less pronounced as compared with those in livers of rats injected with thyroid (fig. 7). The first two features were also somewhat better than in liver cells of rats injected only with progesterone + oestradiol (fig. 8).

Thus, simultaneous administration of all four hormones produced hypertrophic livers of a more normal structure, neutralizing some abnormal features of the livers of rats injected with thyroid (haziness and bluish staining of cytoplasm, indefinite demarcation of cells, and decreased sharpness or dissolution of the basophilic granules).

Effects on Kidneys

The small doses used of oestradiol B.B. did not produce statistically significant changes in weight (tables 1 to 3) or histologic structure (table 5) of the kidneys, except for the increased number of large nuclei ($P < .05$).

Out of three experiments in only one (table 3) did the small dose of thyroid hormone used increase the weight of kidneys significantly ($P < .001$). Histologically, however, all values were found to be greater (tables 5 to 6)—the tubules ($P < .02$), their lumen ($P < .01$), and number of large nuclei ($P < .01$).

Combined administration of these hormones produced a definite ($P < .001$) hypertrophy of the kidneys even in those two experiments, in which thyroid and oestrogenic hormones separately had no significant effect (table 2). In this group the tubules, their lumena and nuclei were greater ($P < .01$, $< .02$ and $< .001$ respectively). The mitoses also occurred in this group in larger number than in the previous groups (table 5).

Androsterone injections caused an increase in weight of the kidneys ($P < .01$, table 3) and larger size of the tubules ($P < .01$, table 6), but no mitoses were found.

Thus, the above mentioned results are in good agreement with those obtained in our previous experiments (9, 18).

Progesterone, injected simultaneously with oestradiol (tables 1 to 3) in one experiment only, when given in larger dose, increased significantly ($P < .01$, table 3) the weight of the kidneys. Histologically, however, in the experiment (table 5) in which there was no significant increase in the weight of the kidneys, the tubules were significantly enlarged ($P < .01$).

Previously (9, p. 338, table 2, line 10) it was found that when there are a large number of mitoses the cells, because of division, might not be enlarged. Probably the cells start to hypertrophy, if they do so, some time after the end of vigorous mitotic division. In support of this possibility it is necessary to mention the experiments on the other organ by Lloyd (23), who obtained very numerous mitoses in uterine epithelium of ovariectomised rabbits on the fourth day after commencement of progesterone injections, but very few on the fifth day.

Hence it is possible to meet cases, just after the end of mitotic division, when the cells have just finished their multiplication and therefore are still small. At this stage there are no, or few, mitoses. In such cases the increased weight of the organ should be explained by hyperplasia of cells, provided that there is no hyperaemia or oedema.

Most probably such a case occurred in our present experiment III, in which the weight of the kidneys was increased ($P < .01$), but no hypertrophy of tubules or increased number of mitoses were found.

When three or four of the hormones used were administered simultaneously (oestradiol, progesterone and thyroid hormone, with or without androsterone) the weight of the kidneys ($P < .001$), their tubules ($P < .001$), and the number of large nuclei ($P < .001$) were increased. Rare mitoses (table 5) were recorded in the tubules of all the groups containing thyroid and in the progesterone + oestradiol group, and no mitoses in the control and oestradiol groups. However, the number of mitoses, when present, was too small for definite conclusions to be made.

Effects on Adrenals

In our previous paper (19) the literature on the subject was reviewed and we described the effect on the adrenals of ovariectomy, androsterone, different doses of oestradiol B.B., and thyroid hormone, administered separately or in different combinations.

These results have been confirmed in the present paper. Thus androsterone decreased the adrenals ($P < .05$, table 3), while oestradiol or thyroid hormone, administered in the small doses used, increased their relative weight ($P < .05 - < .01$, tables 2 and 3). The effect of combined administration of oestradiol + thyroid hormone was greater ($P < .001$, tables 1 and 2). Histologically, androsterone decreased the size of the cortex and the fasciculata cells and their nuclei (figs. 11 and 17); thyroid hormone and oestradiol B.B. administered separately enlarged the cortex ($P < .05 - < .01$, table 7) and the fasciculata cells and the number of large nuclei ($P < .05$, table 7, and fig. 12). The effect was more pronounced when the last two hormones were given together ($P < .01 - < .001$, table 7).

The same effects as before were observed on distribution of lipoid granules in the cortex. Depletion of these granules, varying in degree, was observed in androsterone-injected rats (fig. 17), but no change was found in rats treated with small doses of oestradiol and thyroid hormone (fig. 16) given separately or together.

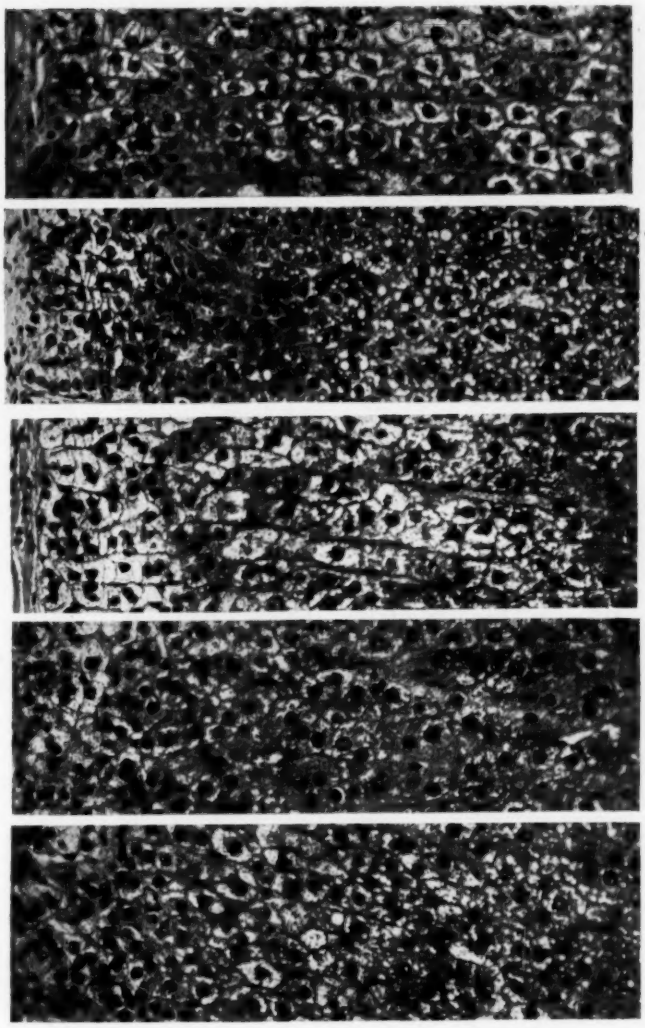
Progesterone injected together with the small dose of oestradiol B.B. (tables 2 and 3) significantly enlarged the adrenals only in experiment III ($P < .02$, table 3). The cortex was larger in all experiments ($P < .02$, table 7), and also fasciculata cells and the number of large nuclei in these cells ($P < .02$, table 7 and fig. 13), without any change in lipoid granule content (fig. 18) or with a slight decrease of the same in the reticularis zone (fig. 19).

After administration of progesterone, oestradiol, and thyroid hormones, with or without androsterone, the adrenals were of about the same size and weight as seen after simultaneous administration of only oestradiol and thyroid hormones ($P < .01 - < .001$, tables 2 and 3). The size of the cortex ($P < .001$, table 7) was also increased to about the same degree.

The size of the fasciculata cells was increased in rats treated with a combination of oestradiol, thyroid hormone, and progesterone ($P < .001$, table 7), but not so definitely after administration of all four hormones (fig. 14). With this combination of hormones, however, a neutralizing effect of the remaining three hormones was clearly demonstrated on the androsterone depressing effect, as shown by the size of cells and nuclei in the fasciculata zone (fig. 14 compared with fig. 11). The lipoid content, with this combination, was about normal (fig. 20) or slightly decreased in the lower part of the fasciculata zone and in the reticularis zone (fig. 21). Clausen (4) injected normal rats with 4 mg. of progesterone daily. At the end of the experiment the adrenals became much smaller due to decreased size of the fasciculata and reticularis cells and of the reticularis blood sinuses. Selye (26), injecting enormous doses of progesterone (10-15 mg. daily), confirmed the involution of adrenals both in intact and spayed rats.

In our experiments comparatively large doses of progesterone were used, although they were much smaller than those administered by Clausen and Selye. Not only a complete absence of involutionary changes in the adrenals of our rats was found, but, on the contrary, a stimulating effect was recorded. Progesterone, however, was used in combination with other hormones. The discrepancy between our results and those of Clausen and Selye might be explained not only by the neutralizing action of thyroid hormone and oestradiol but also by the difference in size of the doses used: large doses of hormones might easily produce toxic involutionary effects.

In experiments I and II for calculation of the number of cells in transverse sections of the zone fasciculata we used an approximate



PART OF OUTER REGION OF ADRENAL CORTEX. Haematoxylin + Eosin. × 310.

In all photographs can be seen a more or less complete section of fibrous capsule, z. glomerulosa with irregular deposition of cells and nuclei, upper part of z. fasciculata with regular cords of cells.

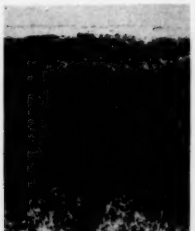
FIG. 10. Control rat. Adrenals 38 mg.

FIG. 11. Rat injected with androsterone. The transitional layer between z. glomerulosa and fasciculata much wider, the fasciculata cells smaller with smaller nuclei. In this rat there is an exceptionally large vacuolation of cytoplasm. Adrenals 32 mg.

FIG. 12. Rat receiving desiccated thyroid. Larger fasciculata cells than in control rats, with occasional large nuclei. Adrenals 64 mg.

FIG. 13. Rat injected with progesterone and oestradiol B.B. Fasciculata cells and nuclei in several cells are larger than those in the controls. Adrenals 49 mg.

FIG. 14. Rat receiving all four hormones. The cells similar to those in control rats. In adrenals of two rats of this group there were occasional mitoses; one can be seen at the upper part of the medium third of the section. Adrenals 54 mg.



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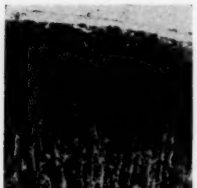

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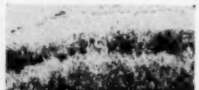

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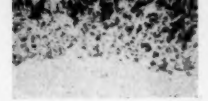

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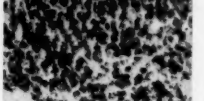

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20

ADRENAL CORTEX, transverse section, ×55.

Lipoids stained with sudan black. From top to bottom of photographs—faintly stained capsule, z. glomerulosa, cords of Z. fasciculata, net of z. reticularis, small part of unstained medulla. Z. glomerulosa is divided from z. fasciculata by a narrow layer of transitional cells, with very little or no lipoid granules (shows light-colored on photographs).

FIG. 15. Control rat. Adrenals 38 mg.

FIG. 16. Rat receiving thyroid. Enlargement of the cortex, all zones well impregnated with lipoid, slight hyperaemia in lower part of fasciculata and in reticularis. Adrenals 56 mg.

FIG. 17. Rat injected with androsterone. Cortex narrower than in controls, partial depletion of lipoid, considerable widening of the layer of transitional cells between glomerulosa and fasciculata. Adrenals 32 mg.

FIG. 18. Rat injected with progesterone and oestradiol B.B. Cortex similar to that in control rats, but larger and with more pronounced lipoid impregnation in z. reticularis. Adrenals 58 mg.

FIG. 19. Rat from the same group as in fig. 18. Poorer lipoid content in z. reticularis than in fig. 18. Adrenals 53 mg.

FIG. 20. Rat receiving progesterone, oestradiol B.B., androsterone, and desiccated thyroid. Enlarged cortex of normal structure, with good lipoid impregnation. Adrenals 63 mg.

FIG. 21. Rat from the same group as in fig. 20. Enlarged cortex, similar to that in fig. 20, but poorer lipoid impregnation in the lower part of fasciculata and in reticularis zones. Adrenals 86 mg.

method, which has previously been described in the section on methods. The results are given in the last column of table 7. They show an increase in two groups only, namely in rats treated with oestradiol and thyroid hormone ($P < .02$) and with these hormones and progesterone (statistically not a significant increase).

Thus, as in our previous paper (19), we must conclude that the hypertrophy of adrenals with more or less normal structure has been obtained after simultaneous administra of all hormones used and that the androgenic involution was prevented in this way.

Effects on Thyroid

In our previous papers the effects on the thyroid of androsterone, oestradiol B.B. in various doses, and thyroid hormone, separately or in combination, have been studied. The literature on the subject has also been reviewed. In the present paper the results previously obtained with these hormones have been confirmed.

Changes in organ weight were statistically not significant. It must, however, be emphasized that even significant changes by themselves alone cannot indicate a hypo- or hyperactivity of the gland, because an increased weight might be due to accumulation of colloid in the case of hyposecretion, or to hypertrophy and hyperplasia of the cells in the case of hypersecretion of thyroid. Therefore histologic changes are the decisive indicators of the condition and function of this gland.

In the present experiments, as before, androsterone (fig. 23) was definitely stimulating to the activity of the gland. As compared with control rats (fig. 22), in the thyroids of rats injected with androsterone the cells became columnar; in places the follicles were lined with two rows of cells, or even sometimes there were aggregates of several rows of cells nearly occluding the lumen of the follicle (e.g., top follicle, second from the left, fig. 23). The amount of colloid was decreased.

Oestradiol alone in the small dose used did not change the structure of the thyroid, while thyroid hormone (fig. 24) depressed its activity, flattening the cells and nuclei and increasing the amount of hard strongly eosinophilic colloid.

Progesterone with oestradiol (fig. 25) had a stimulating effect, similar to that of androsterone. Since oestradiol alone had no effect on the thyroid, the stimulating property must be ascribed to the action of progesterone.

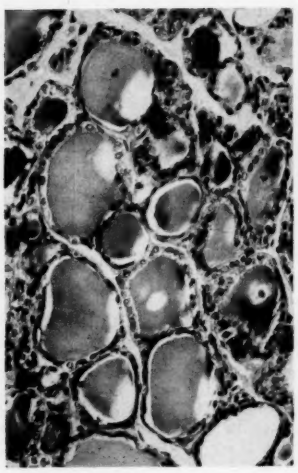
The experiments of Alexiu (1) confirm this conclusion. He experimented upon both intact and ovariectomized rats, injecting 2 mg. of progesterone every day for 90 days; or 2 mg. twice a week for 240 to 360 days. In agreement with our observations, in control ovariectomized rats he observed flattening of epithelium and accumulation of colloid. If the injections of progesterone were made into ovariectomized rats twice a week, stimulation of the thyroid was obtained—high epithelium, small follicles, and small amount of faintly staining colloid. Every day injections, i.e. larger doses, produced severe toxic degenerative changes varying in different follicles and cells from cloudy swelling to necrosis.

The most remarkable difference was obtained with every day injections into normal unspayed rats—no toxic changes were observed but there was the same picture of thyroid stimulation as recorded in ovariectomised rats after fewer injections, twice a week. This obviously indicates that in the normal rat, possessing ovaries, the toxic effects of large doses are prevented, probably by a normal balance of other hormones which becomes upset by ovariectomy. Apparently this preventive effect cannot be explained by the action of oestradiol, since in Alexiu's experiments the effect of large doses of oestradiol benzoate (0.5 mg. daily or twice a week) had an effect similar to that produced by the large doses of progesterone. Alexiu did not perform the experiment with simultaneous injections of these hormones.

In our present experiments when three or (fig. 26) all four hormones were administered, progesterone alone or together with

androsterone prevented definitely, although only partially, the severe depressing action of thyroid hormone on the thyroid gland. Histologically the thyroid in these groups of rats, although more active than in thyroid rats, was similar to that of the control ovariectomised rats (fig. 22), which have a less active gland than normal rats (Korenchevsky and Jones, 19, p. 131, figs. 38 and 39).

Thus the depressing effect on the thyroid



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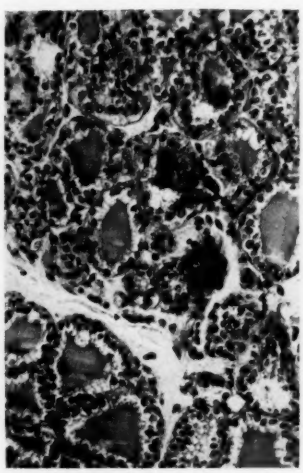

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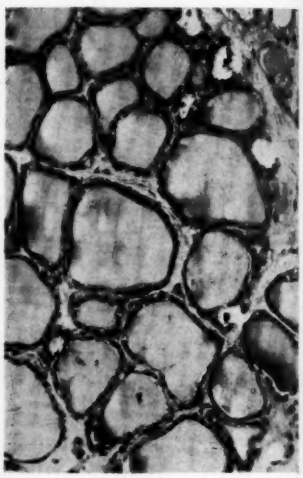

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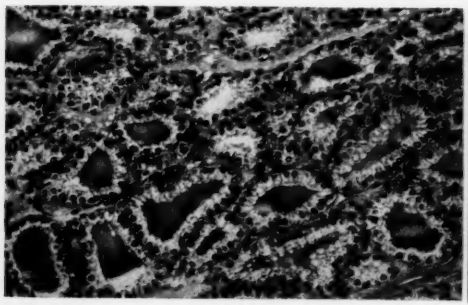

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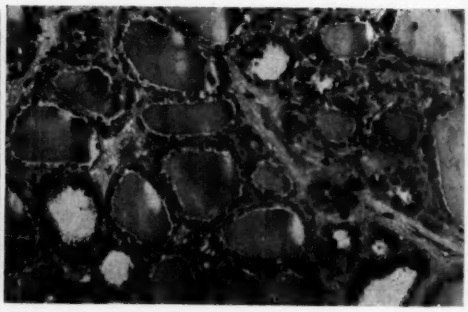

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THYROID, Haematoxylin + Eosin. ×180.

FIG. 22. Control rat. Cubical or flattened cells. Large amount of hard eosinophilic colloid in most follicles. Thyroid 18 mg.

FIG. 23. Rat injected with androsterone. Columnar epithelium, in places (upper left corner) forming solid aggregates of cells nearly occluding the intrafollicular lumen. Amount of colloid decreased. Active gland. Thyroid 18 mg.

FIG. 24. Rat receiving desiccated thyroid. Very low flattened epithelium with flattened nuclei, and large amount of hard colloid. Depressed activity of thyroid (18 mg.).

FIG. 25. Rat injected with progesterone and oestradiol. Active gland similar to that in fig. 23. Thyroid 20 mg.

FIG. 26. Rat receiving progesterone, oestradiol B.B., androsterone, and desiccated thyroid. As compared with fig. 24, a partial recovery of activity of the gland is seen. Mostly cubical cells with round nuclei and amount of colloid similar to those in control rat (fig. 22). Thyroid 22 mg.

gland of thyroid hormone is stronger than the stimulating action of androsterone and progesterone combined. However, since these stimulating and neutralising properties are definite, it is desirable to investigate whether during treatment with thyroid hormone a simultaneous administration of androgens and, in the case of females, progesterone might be useful.

Effects on Weights of Preputial Glands, Hypophysis, Thymus, Spleen, and Heart

In these organs the histologic examination has not been completed and therefore only the changes in weights of these organs will be discussed.

Effect on Preputial Glands.—As in the previous experiments (10, 11, 16, 18) the preputial glands have been obviously hypertrophied after androsterone injection, but no significant changes have been obtained after administration of oestradiol and thyroid hormones or simultaneous administration of the two latter hormones. Also no significant increase was found after administration of progesterone with oestradiol, but a definite hypertrophy was recorded after simultaneous administration of oestradiol, progesterone, and thyroid hormone ($P < .01$, table 2), and of course much more so with, and because of, the addition of androsterone (table 3). Selye (26) claimed that very large daily doses of progesterone alone (10-15 mg.) caused considerable enlargement of the preputial glands.

Effect on Hypophysis.—It is well established that oestrogens in nontoxic doses produce enlargement of the hypophysis, while large doses of this hormone cause tumourlike pathologic changes in this gland. The review of the literature on the subject and the results of our own experiments were given in the previous papers (11, 16, 18). Brooksby (3) found that in female ovariectomised rats progesterone alone had no

Table 1. Experiment I. Effects of Progesterone, Oestrogenic and Thyroid Hormones on Actual Weights of Organs

Doses of hormones: Desiccated thyroid 65 mg. 3 times a week; Oestradiol B.B. 0.028 mg. during first week only; Progesterone 2 mg. daily injected during last 19 days of experiment.

Organs	Controls	Thyroid desic.	Oestradiol B.B.			
			Alone	+ Thyroid desic.	+ Progesterone	+ Progesterone + Thyroid desic.
Abdominal fat (gm.)	15.6	10.2	12.7	6.4	12.9	8.6
Uterus (mg.)	35	38	225	234	236	215
Vagina (mg.)	186	200	347	334	379	371
Preputial glands (mg.)	60	55	53	65	64	71
Adrenals (mg.)	50	59	55	71	55	81
Thyroid (mg.)	16	17	18	17	18	18
Hypophysis (mg.)	11.9	12.4	13.2	12.9	14.3	12.0
Thymus (mg.)	245	324	233	248	179	212
Liver (gm.)	6.87	7.62	6.23	7.81	8.16	9.96
Kidneys (gm.)	1.45	1.62	1.44	1.76	1.57	1.95
Spleen (mg.)	446	962	672	660	683	1085
Heart (mg.)	800	922	802	902	859	941
Final bodyweight (gm.)	279	270	255	240	270	265
Gain or loss in bodyweight (gm.)	+4	−12	−23	−24	−13	−24
Number of rats in each group	4	4	4	5	7	7

TABLE 2. POOLED EXPERIMENTS I AND II. EFFECTS OF PROGESTERONE, OESTROGENIC AND THYROID HORMONES ON RELATIVE WEIGHTS OF ORGANS PER 200 GM. OF FAT-FREE BODY WEIGHT

Doses of hormones: Desiccated thyroid 65 mg. 3 times a week; Oestradiol B.B. 0.028 mg. during first week only; Progesterone 2 mg. daily, injected during last 19 days of experiment.

Organs	Controls	Thyroid desic.	Oestradiol B.B.			
			Alone	+ Thyroid desic.	+ Proges-sterone	+ Thyroid desic. + Proges-terone
Abdominal fat (gm.)	13.5	8.4	11.1	7.6	11.0	7.1
Total body fat (gm.)	48.3	32.0	36.4	25.5	38.4	24.8
Uterus (mg.)	32	32	218	221	214	204
Vagina (mg.)	151	169	316	316	309	309
Preputial glands (mg.)	43	46	48	55	60	70
Adrenals (mg.)	43	50	57	68	51	69
Thyroid (mg.)	14.2	14.1	15.4	15.6	15.7	15.3
Hypophysis (mg.)	9.9	9.9	13.4	12.3	12.3	10.7
Thymus (mg.)	200	274	202	206	143	153
Liver (gm.)	6.32	6.42	6.44	7.09	7.23	8.18
Kidneys (gm.)	1.30	1.36	1.47	1.66	1.43	1.70
Spleen (mg.)	478	812	600	619	532	811
Heart (mg.)	688	776	747	816	734	795
Final body weight (with fat, gm.)	278	270	251	246	261	248
Gain or loss in body weight (gm.)	+16	−12	−17	−24	−13	−26
Number of rats in each group	9	4	8	9	11	12

effect on the weight of the hypophysis, but, when given simultaneously with oestrone, it increased the hypertrophying effect of the latter hormone on this gland. In his experiments both oestrone and progesterone, when injected alone or together, were able to prevent those histologic changes in hypophysis which appear after ovariectomy. Cutuly (6) also found that progesterone did not produce definite changes in weight of hypophysis of female ovariectomised rats. Contrary, however, to Brooksby he could not prevent or correct the gonadectomy changes in this gland.

In our present experiments the hypertrophying effect of oestrogens was recorded in all groups in which oestradiol was present ($P < .05$, - $< .001$), except that (table 3) in which androsterone was also given. The enlargement of the hypophysis, however, was small because of the small dose of this hormone used.

Simultaneous administration of thyroid hormone and progesterone did not change the oestradiol effect, contrary to the observations of Brooksby. Usually androsterone in large doses produces a slight decrease in size of the hypophysis in ovariectomised rats (16). This effect was also recorded in the present experiments ($P < .05$, table 3) when androsterone was injected in the form of crystalline emulsion.

The neutralising effect of androsterone on oestrogenic hypertrophy of hypophysis was especially clear when large doses of oestradiol were used (16). It was not observed in the experiments (18) in which such small doses of oestradiol were used that only a slight increase in weight of the hypophysis was produced. In the present experiments (table 3), however, this neutralising effect of androsterone was evident ($P < .05$) in spite of the small doses of oestradiol B.B.

(compare the weights of the hypophysis in the two last columns of the table 3). Most probably this result can be explained by the fact that injections of androsterone in crystalline form had a stronger effect.

Effect on Thymus.—The review of the literature on the effects of gonadectomy and sex hormones on the thymus and the results of the experiments performed have been given in the previous papers (18, 25).

In the present experiments the involutionary effect of androsterone was confirmed ($P < .01$). The small dose of oestradiol B.B. used had no effect when used alone (table 2), but in combination with progesterone it produced an involution of the organ ($P < .02$, tables 1 to 3). Therefore it must be concluded that progesterone also has an involutionary effect on the thymus. The effect of thyroid hormones on the weight of the thymus in these or in the previous experiments (17, 18) was not clearly evident. In any case, it does not produce any involution, but in some cases, on the contrary, a significant increase in weight (e.g. $P < .05$, tables 1 and 2).

Effects on Spleen.—The spleen became significantly increased in weight after administration of thyroid hormone alone ($P < .01$), or in combination with progesterone and oestradiol ($P < .01$, tables 1 and 2), or when all four hormones were given ($P < .05$, table 3). Therefore thyroid hormone must be considered as the main factor responsible for hypertrophy of the spleen in the groups in which the above mentioned combinations of hormones were given. The hypertrophying property of sufficiently large doses of this hormone on the spleen was emphasize and the literature reviewed in the previous papers (17, 18).

Effects on Heart.—As in the previous papers (10, 16, 17, 18), in the present paper an increase in weight of the heart was obtained after administration of androsterone ($P < .01$) and thyroid hormone when given

TABLE 3. EXPERIMENT III. EFFECTS OF PROGESTERONE, OESTROGENIC, ANDROGENIC, AND THYROID HORMONES ON RELATIVE WEIGHTS OF ORGANS PER 200 GM. OF FAT-FREE BODY WEIGHT

Doses of hormones: Desiccated thyroid 60 mg. 3 times a week; Oestradiol B.B. 0.015 mg. injected 3 times during first week only; Androsterone 10 mg. and Progesterone 10 mg. injected every eighth or tenth day.

Organs	Controls	Androsterone	Thyroid desic.	Progesterone	
				+ Oestradiol B.B.	+ Oestradiol B.B. + Androsterone + Thyroid desic.
Abdominal fat (gm.)	11.0	13.6	7.1	12.6	10.2
Total body fat (gm.)	35.5	43.6	21.7	39.3	32.4
Uterus (mg.)	57	71	46	311	332
Vagina (mg.)	175	293	239	401	417
Preputial glands (mg.)	55	181	71	65	215
Adrenals (mg.)	44	34	59	59	62
Thyroid (mg.)	17.6	17.0	19.3	17.9	19.5
Hypophysis (mg.)	16.3	12.7	15.3	18.6	14.4
Thymus (mg.)	280	190	286	144	146
Liver (gm.)	6.08	7.50	6.80	8.21	7.79
Kidneys (gm.)	1.15	1.44	1.56	1.42	1.69
Spleen (mg.)	842	768	984	809	1000
Heart (mg.)	670	730	905	777	831
Brain (gm.)	1991	1903	2151	2056	1977
Final body weight (with fat, gm.)	240	247	215	237	236
Gain in body weight (gm.)	+27	+36	+4	+22	+6
Number of rats in each group	5	5	5	5	5

TABLE 4. EXPERIMENT I. EFFECTS OF PROGESTERONE, OESTROGENIC AND THYROID HORMONES ON LIVER CELLS

Groups of Rats	Actual Weight of Liver (gm.)	Weight of Paper Replica of Average Cell (mg.)	Percentage of Large Cells	Percentage of Large Nuclei	Number of Mitoses in Standard Area*
I. Controls	6.87	5.70	4.6	14.8	0
II. Thyroid dessic.	7.62	5.91	9.4	47.5	0.2
III. Oestradiol B.B.	6.23	6.53	13.7	28.6	0
IV. Oestradiol B.B. +Thyroid desic.	7.81	6.09	9.9	37.6	3.0
V. Oestradiol B.B. +Progesterone	8.16	7.39	27.9	46.6	0
VI. Oestradiol B.B. +Progesterone +Thyroid desic.	9.96	6.61	17.4	43.4	5.0

* *Note.* The number of mitoses given in the last column represents the average figures from all three pooled experiments. Number of mitoses in the androsterone group was 0, and in the group with all 4 hormones 6.0.

alone ($P < .001$, tables 1 and 3) or in combination with the other hormones used ($P < .02$, - $< .001$, tables 1 to 3).

The small dose of oestradiol in combination with progesterone produced a significant increase ($P < .01$) only in experiment III when a larger dose of progesterone was injected. This injection also resulted in hypertrophy of some other organs (table 3, adrenals and kidneys) which showed no significant change with a smaller dose. Therefore a stimulating effect of larger doses of progesterone on the heart is probable, but a repetition of the experiment is necessary for a definite conclusion to be drawn, especially since oestrogenic hormones alone in suitable doses might also have a cardiotropic effect (18).

SUMMARY

1) Investigation of the weights of organs and fat deposition and histologic examina-

TABLE 5. EXPERIMENT I. EFFECTS OF PROGESTERONE, OESTROGENIC AND THYROID HORMONES ON PROXIMAL KIDNEY TUBULES

Groups of Rats	Actual Weight of Kidneys (gm.)	Weight of Paper Replica of		Percentage of Large Nuclei	No. of Mitoses in Standard Measured Area.
		Average Tubule (mg.)	Average Lumen (mg.)		
I. Controls	1.45	4.82	1.14	8.3	0
II. Thyroid dessic.	1.62	6.36	1.47	26.9	0.3
III. Oestradiol B.B.	1.44	6.08	1.24	19.7	0
IV. Oestradiol B.B. +Thyroid dessic.	1.76	6.44	1.60	43.2	1.4
V. Oestradiol B.B. +Progesterone	1.57	6.24	1.57	18.2	0.2
VI. Oestradiol B.B. +Progesterone +Thyroid dessic.	1.95	7.01	1.54	47.8	0.7

TABLE 6. EXPERIMENT III. EFFECTS OF ANDROSTERONE, PROGESTERONE, OESTRADIOL B.B., AND THYROID HORMONE ON PROXIMAL KIDNEY TUBULES

Groups of Rats	Actual Weight of Kidneys (gm.)	Weight of Paper Replica of Average Tubule (mg.)
I. Controls	1.18	6.93
II. Androsterone	1.45	8.70
III. Thyroid desiccated	1.51	8.39
IV. Progesterone + Oestradiol B.B.	1.40	7.25
V. Androsterone + Thyroid desic. + Progesterone + Oestradiol B.B.	1.73	8.46

tion of uterus, vagina, liver, kidneys, adrenals, and thyroid were made in 78 ovariectomised rats in order to study the effects of progesterone in combination with oestradiol benzoate-butyrate, androsterone, and thyroid hormone on the accelerated process of aging produced by gonadectomy, i.e., on the artificial premature climacteric of rats.

2) In good agreement with the results obtained and conclusions made in our previous papers in this JOURNAL, the stimulating, depressing, or correlative properties of androsterone, oestradiol B.B., and thyroid hormone both on weight and histologic structure of organs examined have been confirmed by the present experiments. Therefore the respective conclusions are not repeated here. It is necessary to add only that, when androsterone was injected as a suspension of crystals its stimulating effect on the thyroid gland was more pronounced than with the oily solution.

3) Progesterone in combination with oestradiol B.B.: a) had a definite stimulating action on the thyroid gland, liver, and adrenal cortex; b) accelerated involution of the thymus; c) prevented appearance of pathologic oestrogenic metaplasia of uterine epithelium; d) when injected in the form of an emulsion of crystals, apparently had more pronounced progestational effect on the uterus and vagina than the oily solution.

4) Correlative effects of progesterone and oestradiol with thyroid hormone were noticeable in an increased hypertrophy of liver and preputial glands; and in a partial neutralising action of progesterone on depression of the thyroid gland produced by small doses of thyroid hormone.

5) Correlative effects of androsterone

TABLE 7. POOLED EXPERIMENTS I AND II. EFFECTS OF PROGESTERONE, OESTROGENIC AND THYROID HORMONES ON ADRENALS (AVERAGE SIZE OF MEDULLA AND CORTICAL ZONES, AND AVERAGE SIZE AND NUMBER OF FASCICULATA CELLS)

Groups of Rats	Weight (mg.) of Paper Replica of					Weight of Paper Replica of Average Fasciculata Cell	Average number of Fasciculata Cells (thousands)
	Medulla	Glomerulosa	Fasciculata	Reticularis	Cortex		
I. Controls	158	57	350	190	572	4.05	17,9
II. Thyroid desic.	171	66	369	283	717	4.51	18,8
III. Oestradiol B.B.	154	43	345	301	689	4.52	17,4
IV. Oestradiol B.B. +thyroid desic.	162	42	426	357	814	4.62	20,9
V. Oestradiol B.B. +progesterone	162	50	323	290	664	4.60	16,1
VI. Oestradiol B.B. +progesterone +thyroid desic.	160	48	405	347	800	4.74	19,5

with the three other hormones used were indicated by a slightly better development of uterus and vagina, intensification of progestational changes in uterine epithelium, less mucification in vaginal epithelium, greater enlargement of preputial glands, more normal appearance of the liver cells, a decrease in the depressing action of thyroid hormone on thyroid gland, and a decrease of oestrogenic hypertrophy of the hypophysis.

6) The neutralising effect of oestradiol and thyroid hormone on androgenic hypoplasia of adrenals, previously recorded by us, was confirmed in the present experiments.

7) Thus, the present results of simultaneous administration of four hormones used confirmed the conclusion previously made, that more normal hypertrophic and histologic changes develop in the organs, affected by aging hypoplasia after plurihormonal treatment as compared with those produced by treatment with a single hormone.

8) The plurihormonal treatment used not only stopped the aging involution of some organs but, moreover, it was able to return the relative weights and apparently also the histologic structure of these organs to the level observed at a younger age. In this very limited sense the plurihormonal treatment used seemed to have a certain anti-aging effect on the climacteric rats.

9) It is necessary, however, to emphasize strongly that to define any agent as a true anti-aging factor, investigation of the changes in weight and histologic structure of some organs is very far from being sufficient. For this purpose, both experimental and clinical, manifold and prolonged morphologic, biochemical, and physiologic experiments are necessary on the effects of the factors concerned on the aging organism as a whole and on all aging features in all organs and tissues.

10) It is obvious that a complete picture of plurihormonal treatment on the process of aging can be obtained only after using a combination of all the main hormones, especially including those of the adrenal cortex and hypophysis.

Ciba, Ltd., supplied the sex hormones used in the experiments and Messrs. Burroughs and Wellcome supplied the desiccated thyroid.

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Submitted for publication October 21, 1947

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The Effect of Arteriosclerosis on the Dynamics of Hypertension in the Aged

A Preliminary Clinical and Pathological Study of 150 Cases

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BLOOD PRESSURE STUDIES HAVE BEEN MADE ON 150 ELDERLY PERSONS AND CORRELATED WITH THE FINDINGS AT NECROPSY. FACTORS INFLUENCING BLOOD PRESSURE ARE EVALUATED WITH EMPHASIS ON THE EFFECT OF THE SCLEROTIC AORTA AND ITS BRANCHES IN PRODUCING THE LOW DIASTOLIC PRESSURES OFTEN FOUND IN AGED INDIVIDUALS.

PREVIOUS studies of blood pressure in the aged have pointed out the following phenomena:

1. An increasing systolic blood pressure with age (10, 11). This has been noted when the systolic blood pressures of large numbers of persons of different age groups have been averaged. We are, however, aware of no data which demonstrate this progressive rise in systolic pressure in large numbers of individuals. On the contrary, Bechgaard (1) followed hypertensive patients from four to eleven years and found the blood pressure levels in each person at the end of the study little altered. We are of the opinion that most observations of large numbers of individuals have not covered a long enough period of time to demonstrate this progressive rise conclusively.

2. Relatively little change in the diastolic pressure with age, when studied under similar conditions, i.e., as the average diastolic pressure of large groups of individuals of different ages. Observers have differed as to whether there is a small increase, no significant change, or a small decrease (10, 11), but it should be pointed out that these average figures should be considered in the light of the two following observations: the number of persons with systolic and diastolic hypertension increases with age (7), and the number of persons with abnormally low diastolic pressure also increases with age (11). It is obvious that these two groups, which are of considerable magnitude, would tend to counteract each other when included in a large statistical series.

3. An increasing pulse pressure with age (10, 7).

4. An increasing incidence of systolic hypertension with age (11), i.e., an elevated systolic blood pressure with a normal or low diastolic pressure also increases with age 11) feel that this type of hypertension is to be sharply distinguished from systolic and diastolic hypertension, that it carries a particularly benign prognosis, and that in fact it may be considered as part of the normal process of aging. One writer feels that it even exerts a beneficial effect on the circulation. Others make no distinctions and include these persons as cases of essential hypertension (1).

5. An increasing incidence of systolic and diastolic hypertension (7, 11), although the increase is not as marked as the rise in incidence of systolic hypertension. On the whole the level of diastolic pressures reached in aged hypertensive patients is not as high as in younger individuals. Malignant hypertension is not observed in the aged. It has often been remarked how well and how long a severe blood pressure elevation is tolerated by old people, especially aged females.

In view of these varied manifestations it is easy to see why there has been so much difficulty and difference of opinion in deciding

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what is the "normal" blood pressure in old age. In studying the cardiovascular system in old persons, as part of a program designed to make the structural and functional diagnosis of arteriosclerosis more precise, we have come to believe that the establishment of what constitutes normal blood pressure in the aged, if this question has any meaning at all, cannot be accomplished by overall statistical studies.

The blood pressure at all ages is the result of the changes in several main variables: the cardiac output, the peripheral resistance, and the elasticity and volume of the larger arteries. Changes in one or two of these variables may be compensated for by changes in the others. It is particularly true of the aged that such changes in multiple variables occur commonly. In youth and middle age alterations in peripheral resistance account for most of the variability in blood pressure, whereas in old age modifications in the larger arteries enter the picture more prominently. But at all ages, as has been emphasized by Wiggers (14, 15, 16) and others (13), fluctuations in all the variables concerned must be taken into account if a true dynamic picture of the circulation is to be obtained.

It was accordingly decided to study a number of aged individuals from this point of view. As a first step, the attempt has been made to obtain clinical and pathologic correlations by comparing the autopsy findings of 150 patients, with their clinical course, as observed over a long period of time. The patients were residents of the Home for Aged and Infirm Hebrews of New York City and therefore represented a selected group in several respects. They were all Jewish. They were all 60 years of age or older. They were people who for one reason or another needed the protection of institutional life. Other than this, there was no selection, since the clinical records of the first 150 autopsies at the Home were chosen without reference to associated diseases or the primary cause of death (the autopsy percentage at the Home is over 90 per cent).

The series included 66 males and 83 females, ranging in age from 60 years to 92 years. There were 23 in the seventh decade, 73 in the eighth, 48 in the ninth, and 4 in the tenth at the time of death. The age at time of first observation and sex distribution is represented in table 1, at death in table 2.

The patients were observed over periods lasting from a few days to twenty years, the average being five and five-tenths years (to the nearest half year), this being the average life expectancy after entrance into the Home. From one to fifty-seven blood pressure esti-

TABLE 1. AGE AND SEX DISTRIBUTION WHEN FIRST OBSERVED

Age Groups	Males	Females
50–60	1	1
60–69	27	36
70–79	28	39
80–89	10	9
90 and over	0	1
	66	83

TABLE 2. AGE AND SEX DISTRIBUTION AT DEATH

Age Groups	Males	Females
50–60	0	0
60–69	9	14
70–79	31	42
80–89	25	23
90 and over	1	3
	66	83

mations were recorded on each patient. These were taken during routine periodic physical examinations and during illness. Seventy-eight patients had six or more blood pressure readings. The blood pressures were taken by various members of the medical staff. No attempt was made to secure basal conditions. This may serve as a valid criticism of the data to be discussed, but, on the other hand, the readings so obtained may serve as a truer index of the blood pressures which these people manifested in their daily lives.

When an attempt was made to classify these patients according to the type of blood pressure they manifested, difficulty was encountered in a large number because of the variability of the blood pressure readings. We were interested to find that variability in blood pressure seemed to be as much a characteristic of the aged as of the young. Caution must therefore be exercised clinically in interpreting only one or two blood pressure readings in old people, especially when not taken under basal conditions.

For purposes of classification readings of 150 mm. Hg. systolic, 90 mm. Hg. diastolic or lower, were termed normal; readings over 150 systolic with diastolic pressures 90 or lower, systolic hypertension; and readings over 150 systolic, 90 diastolic, systolic and diastolic hypertension. The following results were obtained:

Group I-a. Eighteen patients, 12 per cent of the total, had a normal blood pressure reading.

Group I-b. Seventeen patients, 11.3 per cent of the total, had predominantly normal blood pressures, with an occasionally hypertensive or diastolic hypotensive reading.

Totalling Groups I-a and I-b, 35 patients, or 23.3 per cent, of the series had normal or predominantly normal blood pressures throughout their course.

Group II-a. Twenty patients, 13.3 per cent of the total, had every reading of systolic pressure elevated, every diastolic pressure normal.

Group II-b. Forty patients, 26.7 per cent of the total, had predominantly systolic hypertension, but also had a varying number of normal and/or systolic and diastolic hypertensive readings.

Sixty patients, or 40 per cent, of the series had systolic or predominantly systolic hypertension.

Group III-a. Twenty-five patients, 16.7 per cent of the total, had both systolic and diastolic pressures elevated on every reading, except terminally.

Group III-b. Seventeen patients, 11.3 per cent of the total, had predominantly systolic and diastolic hypertension, with a variable number of normal and of systolic hypertensive readings.

Forty-two patients, or 28 per cent, of the series had systolic and diastolic or predominantly systolic and diastolic hypertension.

Group IV. Thirteen patients, 8.7 per cent of the total, had mixed blood pressure readings, which were not readily classifiable into the previous groups.

These results are summarized in table 3, which also includes the relative sex incidence. Whereas the relative sex incidence was approximately the same in the systolic hypertensive group as in the group as a whole, males predominated in the normal group and females in the systolic and diastolic hypertensive group.

For each of the three blood pressure groups the incidence of the following specific anatomical findings was calculated: coronary occlusion, aortic arteriosclerosis, gross renal arteriosclerosis, left ventricular hypertrophy, and cerebral accidents. In the males there was no significant difference in the incidence of coronary occlusion in the three groups. One-third of all the men observed suffered from coronary occlusion. None of the females with normal blood pressures had coronary occlusion, whereas those with both types of hypertension had a definitely lower incidence than the males.

Since the statement has been made that the occurrence of coronary occlusion in females is unusual in the absence of either diabetes or hypertension, the incidence of diabetes was determined. There were only three

TABLE 3. NUMBER OF PERSONS OF EACH SEX IN BLOOD PRESSURE GROUPS

	Males	Females	Ratio M/F	Total Number	Total Per Cent
Group Ia	11	7		18	12
Group Ib	12	5		17	11.3
Group I	23	12	66/34	35	23.3
Group IIa	5	15		20	13.3
Group IIb	19	21		40	26.7
Group II	24	36	40/60	60	40
Group IIIa*	7	18		25	16.7
Group IIIb	5	12		17	11.3
Group III	12	30	29/72	42	28
Group IV	8	5		13	8.7
Total	67	83	45/55	150	100

diabetic males and three diabetic females who developed coronary occlusion. All three of the females had systolic hypertension. Systolic hypertension in aged females is associated with coronary occlusion at least as often as systolic and diastolic hypertension. One-fourth of all the females observed suffered from coronary occlusion.

The percentage incidence of mild, moderate, and severe degrees of arteriosclerosis of the aorta in the three groups was determined and showed the following relationships. While all groups showed a striking incidence of aortic sclerosis the occurrence of the severe grade was highest in the systolic hypertension group. The severe grade was found least often in the normotensive group.

The gross evidence of renal arteriosclerosis was somewhat more pronounced in hypertensive groups than in normotensives, with the severer grades more prominent in the systolic-diastolic hypertension group. In respect to renal arteriosclerosis, therefore, as with aortic arteriosclerosis, the findings are in the direction one would expect theoretically, but all degrees of both conditions are found distributed throughout all three groups. The significance of this will be discussed later. The findings are similar to the above in that the incidence and severity of left ventricular hypertrophy increase as one ascends the hypertensive scale.

The occurrence of cerebral accidents was determined on clinical grounds since few brains were obtained postmortem. The clinical diagnosis was only made definitely in the presence of frank paralysis. The incidence increased as the hypertensive scale was ascended. The number of cases was too small to determine the relative sex incidence with reliable accuracy.

The various degrees of aortic atherosclerosis were correlated with pulse pressure. Although there is a tendency for the pulse pressure to vary with the degree of sclerosis, this is by no means a hard and fast rule,

TABLE 4. INCIDENCE OF CORONARY OCCLUSION

	Males Number	Males Per Cent*	Females Number	Females Per Cent	Total Number	Total Per Cent
Group I	7	30	0	0	7	20
Group II	8	33	9	25	17	28
Group III	4	33	7	23	11	26
Group IV	3	37.5	0	0	3	23
Total	22	33	16	19	38	25

* Percentage of males with normal or predominantly normal blood pressures who had coronary occlusion; similarly for the other percentage figures.

since aortic inelasticity and sclerosis are not necessarily related and since changes in other circulatory variables besides the elasticity of the aorta enter into the determination of the pulse pressure, as other authors have pointed out.

DISCUSSION

The blood pressure is mainly determined by four variables: the cardiac output, peripheral resistance, aortic elasticity, and capacity. Clinically blood viscosity may be left out of consideration in almost all cases.

1. The Cardiac Output.—Experimental studies by Wiggers have shown that with other variables constant, increasing the systolic discharge increases both the systolic

and diastolic pressure, the systolic to a greater extent than the diastolic, thus resulting in an increased pulse pressure. In old age the following conditions may decrease cardiac output: congestive heart failure, inanition, and myocardial infarction in the acute stage. The reduced blood pressure, commonly found for variable lengths of time following coronary occlusion in 30 to 50 per cent of cases, is probably not due to lowered cardiac output, but to changes in peripheral resistance (8). It should be borne in mind, however, that the cardiac output may be increased in heart failure because of thyrotoxicosis, severe anemia, and emphysema (13).

TABLE 5. INCIDENCE OF AORTIC ARTERIOSCLEROSIS

	Mild	Moderate	Severe
Group I	40%	52%	9%
Group II	23%	43%	33%
Group III	33%	50%	17%

2. Peripheral Resistance.—In Wigger's circulation model, augmenting the arteriolar resistance led to an increase in both systolic and diastolic blood pressure, the rise in the diastolic exceeding that of the systolic, thus producing a decreased pulse pressure. Since a large number of hypertensive patients have an increased pulse pressure, Wiggers (16), Weiss (13), and others have concluded that changes in the aorta and great vessels must be present in these instances, together with increased arteriolar resistance.

3. Aortic Elasticity.—In the circulation model, increasing the peripheral resistance and then reducing the elasticity of the aorta resulted in further increase of the systolic pressure while the diastolic pressure was reduced. Wiggers deduced two important corollaries from this: "(a) Aortic sclerosis or any other factor which reduces aortic distensibility accentuates the elevation of systolic pressure but tends to reduce diastolic pressure. (b) An essentially normal diastolic pressure in hypertension is not necessarily a favorable sign which indicates that peripheral resistance is normal. More often it denotes extension of a process to the larger arteries and particularly the aorta" (14). Wezler and Böger (17) in an exhaustive study of the cardio-vascular system have also emphasized the important role played by the aorta and great vessels, whose walls are composed largely of elastic tissue. They have compared the action of these vessels to an air-pressure chamber (*Windkessel*) in transmitting pressure from the heart to the periphery.

4. Aortic Capacity.—Increase in size of the aorta has the same effect as a decrease in systolic discharge, i.e., either process if superimposed on a primary vasoconstriction tends to reduce systolic pressure more than the diastolic. It should be noted that aortic dilatation and aortic inelasticity both occur as age advances and their effects on blood pressure are in opposite directions.

The diverse and distinctive blood pressure patterns in the aged may be explained on the basis of the foregoing physiologic analysis and the autopsy and clinical findings in the present series in the following manner. As age advances there appears to be a tendency for peripheral resistance to increase. The increased peripheral resistance accounts for the frequent finding of systolic and diastolic hypertension in the aged (18 per cent of males, 36 per cent of females in this series). This hypertension is of the high systolic, relatively low diastolic, high pulse pressure type, because of the second important change with aging (5), decrease in aortic elasticity which is most frequently, but not necessarily, accompanied by other manifestations of arteriosclerosis.

Of interest in this connection is Smithwick's evaluation of the results of sympathectomy for hypertension according to the pulse pressure variations. He found the best results were obtained where pulse pressure was less than half the diastolic pressure. He states, "the wider the pulse pressure the greater the decreased elasticity of the larger vessels, and apparently the less likely the presence of increased tone of arteriolar smooth muscle mediated by the nervous system" (12).

Decreased elasticity of the large vessels may account for the rarity of diastolic pressures over 140 in the aged, for the absence of malignant hypertension in the aged, and for the comparative well-being with which many old people, especially females, tolerate hypertension with systolic levels over 200 mm. Hg., for many years. These observations and our clinical findings are also in accord with the opinion of Levine (6), to whom it has seemed that most cerebral accidents in hypertensive patients have occurred in individuals with pressure levels of 200 to 240 systolic over 100 to 120 diastolic, whereas those with diastolic pressures of 140 to 160 are more apt to develop general encephalopathy. He suggests that the high pulse pressure may be the important factor in causing rupture of a cerebral vessel. An alternative explanation is that the high pulse pressure is merely an indication of generalized advanced arterial change.

When the decrease in elasticity of the aorta occurs to a relatively greater degree than increase in peripheral resistance, a systolic hypertension results. Forty per cent of our patients showed this picture predominantly. On the other hand, decreased aortic elasticity is not the only factor which may be operative in producing increased systolic pressure in older individuals. Over-exertion and nervous influences of various kinds may also cause increased cardiac output.

TABLE 6. INCIDENCE OF GROSS RENAL ARTERIOSCLEROSIS

	Smooth	Finely Granular	Finely Granular with Cortical Narrowing	Column Two Plus Three
Group I	40%	30%	9%	39%
Group II	35%	48%	12%	60%
Group III	36%	38%	26%	64%

Wigger's warning that a normal diastolic pressure with an elevated systolic pressure may not necessarily represent a normal peripheral resistance deserves more clinical emphasis. The relatively few cases which have been found to progress from systolic and diastolic hypertension to systolic hypertension is not a valid argument against this view, since the increase in peripheral resistance and the decrease in aortic elasticity probably occur concomitantly in these cases rather than successively. This contention will only be placed on a firm foundation when accurate measurements of the peripheral resistance are made in patients with systolic hypertension.

TABLE 7. INCIDENCE OF LEFT VENTRICULAR HYPERTROPHY

	None	Mild	Moderate	Marked
Group I	49%	11%	40%	0%
Group II	30%	22%	46%	2%
Group III	14%	21%	45%	19%

Finally, "normal" blood pressure in the aged usually does not mean a "normal" cardio-vascular system. Dilatation of the aorta by tending to reduce the systolic, and to a lesser degree, the diastolic pressure will, in many instances, counterbalance the hypertensive effects of increased peripheral resistance or decreased aortic elasticity. This was observed in several of our cases. Probably in many instances cachexia, severe coronary artery sclerosis, and chronic congestive heart failure reduce cardiac output, which likewise has a hypotensive effect. After a coronary occlusion or cerebral accident, elevated blood pressure readings may become normal for long periods, or systolic and diastolic hypertension may be converted to systolic hypertension. Some of these changes are probably mediated by alterations in peripheral resistance.

When each of the cases in the present series was subjected to analysis in the light of the above theoretical discussion, in very few instances was it impossible to correlate the blood pressure readings with these interacting factors. For example, only one case of the blood group which had every blood pressure reading normal had a smooth and freely elastic aorta. In this case, a diabetic, marked coronary artery sclerosis and periph-

TABLE 8. INCIDENCE OF CEREBRAL ACCIDENTS

	Number	Per Cent
Group I	2	6
Group II	6	10
Group III	10	24

eral arteriosclerosis necessitating amputation of one extremity were present. In all the others, varying degrees of loss of elasticity of the aorta were counterbalanced by dilatation of the aorta or by factors tending to reduce cardiac output.

Russek and Zohman (11) have found that the prognosis of aged males with systolic and diastolic hypertension is worse than for males with systolic hypertension or normal blood pressures. Bechgaard (1), however, has shown that the prognosis becomes relatively better as age advances and that hypertensive males over 70 years of age have only a slightly increased mortality whereas hypertensive females aged over 70 years have no increased mortality.

Furthermore, the condition of the heart was one of the main indices determining the prognosis. Although the present series was too small for the determination of mortality statistics, the findings did show that systolic and diastolic hypertensive patients in general had a tendency toward more severe vascular involvement (higher incidence of cerebral accidents, cardiac hypertrophy, and renal involvement). On the other hand, this difference was not very pronounced and all degrees of involvement of heart, great vessels, and kidneys were found in all three groups. Of significance is the finding that the incidence of coronary occlusion in females was approximately the same for systolic and diastolic hypertensive patients as for systolic hypertensives while no instance of coronary occlusion was found in females with normal blood pressure. In males the incidence in all three groups was approximately the same.

Our studies seem to indicate that the finding of an increased pulse pressure probably means decreased aortic elasticity and concomitant sclerosis, in the absence of such factors as heart block, hyperthyroidism, Paget's disease, or other conditions increasing cardiac output. On the other hand, a normal pulse pressure does not necessarily, and usually does not, mean a normally elastic aorta, owing to the compensatory factors discussed above. It is our aim to amplify these preliminary correlations by the application of exact physiologic measurements of the cardiac output and peripheral resistance.

SUMMARY

As age advances, there is a tendency for peripheral resistance to increase, for aortic elasticity to decrease, for aortic volume to increase, and for cardiac output to decrease. The blood pressure will reflect which of these factors predominate. A "normal" blood pressure in old age is not evidence of a normal cardio-vascular system, but is the result of several of the above factors acting in opposite directions.

Systolic hypertension is not to be sharply distinguished as a special form of elevated blood pressure, entirely normal for old age, and benign. Its presence, for example, is associated frequently enough with coronary artery disease that coronary occlusion in females is as common in this group as in the systolic and diastolic hypertensive group. The findings in this series are compatible with the concept that many cases of so-called systolic hypertension are in reality a form of systolic-diastolic hypertension, in the sense that peripheral resistance is increased, but the level of diastolic pressure is modified by changes in the great vessels.

Systolic and diastolic hypertension in old age appears to make the persons who manifest it more liable to cerebral accidents and adds a burden to the heart, but our figures show the frequency of similar findings in normotensive and systolic hypertensive aged individuals. Malignant hypertension is rarely, if ever, observed in the aged. The level of blood pressure in old age should not be taken as an index of pathologic involvement of the vascular system but should be supplemented by studies to determine the cardiac

cerebral, and renal function and the degree of elasticity and dilatation of the aorta. Exact physiologic measurements of the cardiac output and peripheral resistance would be particularly desirable.

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Submitted for publication November 10, 1947

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Observations in an Old Age Counselling Center

Preliminary Report on The First 100 Clients

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ONE OF THE MOST IMMEDIATE AIMS OF PSYCHIATRIC GERONTOLOGY IS TO ESTABLISH OLD AGE COUNSELLING CENTERS ANALOGOUS TO THE CHILD GUIDANCE CLINICS. THERE IS AN INCREASING AWARENESS OF THE PROBLEMS OF THE MALADJUSTED ELDERLY INDIVIDUAL LIVING IN THE COMMUNITY, AND PSYCHIATRIC TREATMENT IS BEING DIRECTED TOWARDS MAKING THE PATIENT BETTER ADAPTED TO HIS ENVIRONMENT DURING THE LATER PHASE OF LIFE. DR. STERN ANALYZES THE FIRST HUNDRED CASES ENCOUNTERED IN THE NEWLY ESTABLISHED COUNSELLING CENTER OF THE GERONTOLOGIC UNIT OF THE PSYCHIATRIC DEPARTMENT AT MCGILL UNIVERSITY. HE DESCRIBES THE PRELIMINARY AIMS OF THE COUNSELLING CENTER, THE TYPE OF CASES ENCOUNTERED, AND GIVES TWO CASE HISTORIES TO ILLUSTRATE SOME OF THE MECHANISMS OF MALADJUSTMENT FREQUENTLY FOUND IN THIS AGE GROUP.

THE following is a survey of the first hundred cases seen in a Counselling Center for the Aged. The term "old age" is somewhat misleading since our work included patients of the involutional period and the lower limit was put at the age of 50; we found that the problems of involution cannot be separated from those of old age. The purpose of this survey is only a preliminary description of the chief problems encountered in this age group in a particular social and economic sector of the population. The investigation is at present being followed up by studies of single cases employing more intensive methods of investigation.

Simultaneously with the opening of a Psychiatric Department at McGill University, the Gerontologic Unit was established as one of the research groups of this Department. One of the purposes of this Unit was to study the psychiatric borderline problems of the higher age group in the average population. It has been noted that geriatric psychiatry has hitherto been too much concerned with cases of organic debility which required nothing but custodial care, and that therefore the problems of emotional adjustment arising in borderline situations of that age group have received too little attention (N. Cameron, 5; Lawton, 15). Child Guidance Clinics have opened up the field of the maladjusted child and removed child psychiatry from the area to which it had been restricted, i.e., custody over severe cases of mental deficiency and epilepsy; in the same manner the Old Age Guidance Clinic will eventually enlarge the vista of geriatric psychiatry to a large social and psychologic area, far beyond that of involutional and senile psychoses.

Comparatively few attempts to establish such Old Age Counselling Centers have been made (Lawton, 15; Martin, 18). Apart from these there have undoubtedly been many involutional and old patients in ordinary psychiatric outdoor departments and in such social agencies which had the benefit of a psychiatric consultant, but systematic investigations on a comparative basis are scanty (Barker, 2; N. Cameron, 5; Prout and Bourcier, 24; Robinson, 25; Woltman, 30). Woltman (30) found among 200 geriatric patients 40 about whom a psychiatric diagnosis was made. Of these psychiatric cases 27.5 per cent were considered as psychoneurotic. Prout and Bourcier (24) found 16 neurotic individuals among 100 patients of the involutional period (between 40 and 60) who were admitted to a private psychiatric institution. Barker (2) found

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that 43 out of 240 patients between the ages of 60 and 70 suffer neuroses or affective disorders.

Cameron (5) made the following diagnoses on 50 consecutive patients of a psychiatric outdoor department: hypochondriasis, 23 cases; neurasthenia, 2 cases; anxiety states, 14 cases; neurotic depression, 1 case; paranoid, 1 case; structural disease of the central nervous system, 9 cases. Robinson (25) found 11 cases of psychoneurosis in a group of 119 elderly psychiatric patients. As so often in statistics pertaining to psychiatric classification, these results are hardly comparable because, at least in the non-psychotic groups, the classification is not uniform, and the groups examined do not come from comparable social, racial, and economic groups.

Few observations have been made about the actual pattern of complaint, the symptom choice and the verbalization, as compared to other age groups. Overholser (21) emphasizes the fact that preoccupation with gastrointestinal functions is marked among aged maladjusted individuals and that this is the more remarkable since objective disease is much more frequently found in the cardiac and renal systems than in the digestive one. This may be associated with the theory that the aged return to pregenital forms of satisfaction (Hamilton, 12). It can be demonstrated that the common factors of insecurity in old age are at times only pegs on which the patient fixes his depression, whereas in reality there is a reactivation, after many decades, of infantile or early adult traumatic material (Pearson, 22; Stern and Menzer, 29).

Thus, the nosologic evaluation and the psychologic interpretation of common problems of behaviour and adjustment in the aged are only in an initial stage of development. The same may be said about the technique of counselling and psychotherapy applicable to this group. It is well remembered that Freud taught originally that the higher age group is not accessible to formal psychoanalysis. This was later somewhat modified. Lillien Martin (18), who established the first Old Age Counselling Center in San Francisco in 1929, does not go very specifically into the question of technique. Rogers (26) states that age is an "uncertain factor" when it comes to counselling and psychotherapy and that "careful consideration should be given" to the question of elasticity in clients over 50 years old. He gives the age period of individuals eligible for counselling or psychotherapy tentatively as from 10 to 60. On the other hand he advises environmental or indirect treatment for persons who are "too young or too old, too dull or too unstable, for a direct type of therapy."

Subjects

Age, marital status.—These are indicated in the following tables.

Immigrant Origin.—Fifty-four per cent of the clients were born in the United Kingdom, 25 per cent in Canada, 8 per cent in the United States, and 13 per cent in Europe.

Social and Economic Status.—The social agency is maintained by a Protestant charity organization. The clients are referred to this organization by relatives or friends, by other social agencies, by the Victorian Order

TABLE 1. AGE GROUPS

Age	M	F	Total
Between 50 and 60	4	21	25
60 and over	20	55	75
Oldest age:		86	
Youngest age:		50	
Average age:		64	
Standard deviation:		7.15	

TABLE 2. MARITAL STATUS

Status	M	F	Total
Married	15	14	29
Single	4	18	22
Widowed	3	36	39
Separated	2	8	10

of Nurses (a group of nurses working exclusively in homes), by ministers, doctors, by the social services, or hospitals, and are supported by the Family Welfare Organization in various ways. They are indigent, or they have to be at least partly supported. The Old Age Pension granted by the government is $25.00 per person per month, and only people of 70 or over are eligible. Those who are below this age are supported by the Family Welfare Organization, according to their earning capacity, with money for rent, with food allowances ($14.35 for one person, $25.60 for two persons per month) and with fuel, clothing, or furniture. They are helped and advised in obtaining hospital beds or permanent shelter. Their physical state is regularly checked by a Health Service through which they also obtain prescriptions.

Social History.—As far as their social history is concerned, 16 had experienced a marked downslide during life, from the upper class to economic dependence; 21 had been fairly comfortable but experienced a downslide; and 63 had been born in a working class environment, and after varied experiences ended in various degrees of economic dependence.

Dwellings.—In order to have a clear impression of the social setting of our group, it is necessary to give a brief account of their dwellings. Of the clients 55 lived in rooms with housekeeping privileges; 4 in rooms without cooking privileges; 27 in small flats; 3 in sheltering homes; 4 in boarding houses; 4 were domestic workers living in their place of employment; the whereabouts of 3 were unknown. As the majority of these people lived in housekeeping rooms it might be well to give a composite picture of their living facilities:

> These rooms are in downtown areas characterized by many rooming-houses and the housing standards are correspondingly low. The houses are usually three-storied, and the clients appear always to live on the third floor or in the basement. Cooking facilities usually consist of a two-jet gas burner in the corner of the room, or a complete gas stove in the hall outside the door. Washing is done in the bathroom. There is usually a complete bathroom with a separate lavatory, and this may serve from four to ten people. The room itself is usually small and poorly furnished. Fresh wallpaper appears very infrequently and the ceilings are usually dark gray. The floor is usually covered with linoleum and the furniture consists of a bed, a chest of drawers, a mirror, and a straight-backed chair. Occasionally there is a radio and if the client has lived in a room for some length of time there is usually an incredible amount of odds and ends—pictures, cartons, suit cases, trunks, knickknacks—so that the casual visitor is utterly bewildered. There are rarely adequate cupboards, and clothing hangs on the back of doors. There is rarely any kind of refrigeration, and all perishable goods are usually kept on the window sill.

TABLE 3. REASONS FOR APPROACH TO SOCIAL AGENCY

	No. of Cases
Financial assistance	86
Advice in securing more adequate living arrangements	11
Help in administering income	1
Advice in securing employment	1
Help in marital problem	1

Reasons for Referral to Psychiatrist.—In each case the psychiatric consultant was presented by the social worker with one or several problems, usually stated in concrete terms. The worker wanted to know whether, and how, the client should be employed; whether he should resume relationship with his children; why he kept on changing his abode.

Technique and Aim of Interview and Counselling

The clients are prepared for the first psychiatric interview by their respective social worker. They are told that the Agency has a Counselling Service, conducted by a psychiatrist, which deals with problems of emotional adjustment. Since nearly all clients are aware of the fact that they have such problems they accept the suggestion readily. In some cases it is necessary to omit the word psychiatrist but the introduction of the procedure of counselling is otherwise the same.

The technique of interviewing and of counselling has to be largely modified in a setting such as this. The fact that the one who counsels is frequently much younger than the one who has to take advice creates a psychologically peculiar situation. Moreover, the situation of this particular social and economic group, i.e., the recipients of charity, accentuates the delicacy of the situation. The most profound difference between this and any other situation of counselling, however, is something else. In the psychiatric guidance of younger age groups there is one fundamental aim, to correct previous mechanisms of faulty adjustment with the purpose of helping the subject to mature and to tap his productive resources for the future. In the case of old age groups the factor of irreversibility in the inner and outer situation is often so overwhelming that the very aim of counselling and psychotherapy is changed. The older the patient is the more our aims are confined to the following:

(1) To make the patient's remaining years more peaceful and contented,

(2) To ease the situation for those who have to live with him, and

(3) To appraise the situation clinically for the benefit of the social worker.

This last procedure has an indirect influence on (1) and (2). Indeed, in many cases we confined ourselves to such an appraisal, and these cases were invariably followed up under our direction by the social worker.

If one considers the criteria given by Rogers (26) for the indications of various methods of approach, it becomes obvious why in the majority of our cases the treatment had to be environmental and indirect.

An old person who has become economically dependent will often approach the counsellor with a certain normal degree of suspicion, even after a most careful preparation. Our experience with this group indicated that it was best to keep the style of the interview as much as possible "free." In many cases we followed the procedure advocated by Rogers (26) for certain situations, i.e., not to take the case history ourselves. Nevertheless, in the majority of cases the counsellor was able to obtain a full clinical history himself. In the remaining cases he had to rely on the detailed history given by the social worker and on facts supplemented during the interview. Apart from this the client's case was appraised in the usual way, from his motility and the verbalization of his complaints.

The interview was invariably conducted in the following manner. The patient was asked for the approximate date of his last physical checkup and then about his physical complaints. We found this very useful in overcoming the initial suspicion. Even the most apprehensive patient opens up freely, often with obvious signs of relief, about his physical complaints. Since almost all clients of this age group have somatic complaints and some minor objective disease, this provided a good starting point. The motility and type of verbalization during this part of the interview is diagnostically important.

This led with ease to the discussion of the patient's emotional adjustment. Frequently

the patient did not seem to realize the transition. After all spontaneous complaints had been enumerated the patient was asked leading questions with regard to appetite, digestion, and sleep. With the mention of sleep the interviewer led over to the question of "nerves." This question was formulated in a nonsuggestive way. After this introduction there was no difficulty in allowing the patient to give a spontaneous account of his emotional state. During this, leading questions were avoided as much as possible. In those cases in which the case history was taken it was begun after that second part of the interview. In the other cases only that material in the patient's history which the patient revealed himself was discussed.

For the reasons given above we avoided tests as much as possible and questionnaires altogether. We found, however, that testing and questionnaires are applicable to a selected number of clients. The Rorschach test was given to 41 out of our patients of sixty or over.

TABLE 4. PHYSICAL DIAGNOSES

Diagnosis	No. of Cases
Hypertensive cardiovascular disease	35
Arthritis—extremities	14
Arthritis—spinal	9
Arrested syphilis	5
Cataract	4
Chronic bronchitis	3
Varicose veins	2
Varicose ulcer	2
Phlebitis	2
Cancer—post-operative	2
Glaucoma	2
Menopausal syndrome	2
Valvular heart lesion	2
Paralysis agitans	2
Deafness	1
Defective vision	1
Hemiplegia	1
Cholecystitis	1
Bronchogenic carcinoma	1
Coronary thrombosis	1
Psoriasis	1
Pernicious anaemia	1
Occipital neuralgia	1
Old peptic ulcer—healed	1

OBSERVATIONS

Physical Diagnoses.—The following table shows the frequency of diagnoses within the total group.

Spontaneous Complaints.—In contrast to the diagnostic reports from the Health Center, it is interesting to list the spontaneous complaints as given by the patients themselves, using as much as possible the patients' verbalization. In the order of frequency they were:

Insomnia
Backache, rheumatic pain
Crying spells
Faulty appetite
Depression
Fatigue
Leg trouble
Nervousness
Faulty digestion
Faulty memory
Headache
Shakiness
Tension
Breathlessness
Ear noise
Urinary frequency

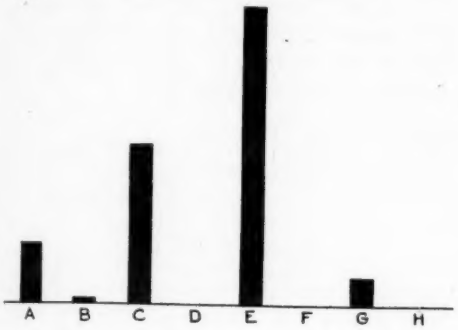
Evaluation.—For the evaluation of the cases the following classification was used:

Psychoses
Organic impairment
Depression
Free anxiety
Phobic anxiety
Conversion symptoms
Compulsive-obsessive symptoms
Simple maladjustment

This evaluation was purely clinical except for the cases in which the Rorschach Test was used as an additional aid. Organic impairment was diagnosed on the basis of impairment of memory for recent events, impairment of retention, coarse impairment of judgment, and the characteristic rapid fluctuation of affect as seen particularly in hypertensive encephalopathy. For the diagnosis of free anxiety the common clinical criteria of anxiety (D. E. Cameron, 4; Grinker and Spiegel, 11; Malamud, 17) were used. The term conversion symptoms is used in the original sense as in conversion hysteria. There is undoubtedly a vast psychosomatic background to the numerous physical ills of old age. However, the scope of the present study did not allow an analysis of the psychosomatic background of the patient's illnesses. This point will be discussed in detail later. The category simple

maladjustment was used in all those cases in which the main symptoms lay in the field of interpersonal relationship, such as undue friction with the environment, isolation from the rest of the family, generally faulty conduct with little or no evidence of symptoms pertaining to the remaining categories. The symptomatology in these cases overlapped to a certain degree with what is in the psychoanalytic literature referred to as character neurosis.

The distribution of cases within our group is illustrated in the following graph:



A - FREE ANXIETY (11)
B - PHOBIA (1)
C - DEPRESSION (29)
D - HYSTERICAL CONVERSION STATES (0)
E - SIMPLE MALADJUSTMENT (54)
F - COMPULSIVE-OBSESSIVE STATES (0)
G - FUNCTIONAL PSYCHOSES (5)
H - ORGANIC PSYCHOSES (0)

GRAPH 1

In this graph each case is put into one single category in spite of a certain amount of overlapping. Thus, for instance, a depressed patient might show signs of organic impairment, or an anxious patient might show signs of depression. With reference to free anxiety, we made a qualitative observation. The pattern of complaints differed as compared to what is commonly seen in younger and middle-aged people. The symptomatology of these states was impoverished. There were no complaints directly referring to the autonomic system, such as palpitations, sweating, hyperstalsis. Instead the patient complained of insomnia, and showed in his motility manifestations of restlessness and tension.

This observation should be followed up by objective tests of autonomic reactions in this age group as compared to younger age groups. Our statistics show that the average age of those patients in whom free anxiety was diagnosed is 57 years with a standard deviation of 5.05, as compared with the average age of the total group, 64 years, with a standard deviation of 7.15. The smallness of the sample of the patients with the diagnosis of free anxiety (11) does not allow any conclusions from this statistical difference. Phobic anxiety was practically absent in the entire group.

The depressions were usually reactive ones, with very obvious immediate content such as loss of a near relative. This, however, was often superimposed on a long history of maladjustment, and had some of the characteristic features of reactivation described before (Stern and Menzer, 29). The absence of compulsive-obsessive trends and the absence of conversion symptoms among this group is noteworthy. The psychotic patients all suffered from functional psychoses. There was not a single case of organic psychosis associated with aging in the total group. Whenever there were organic signs present, they presented only a superimposed feature and not the nucleus of the patient's disturbance. The most conspicuous element was that of simple maladjustment. These patients were not referred to us because of subjective complaints pertaining to emotional difficulties but the social worker found one or several of the following symptoms:

(a) The patient had severed relations with his or her children, or these relations had become difficult.

(b) The patient changed his abode frequently. Often these patients move restlessly from one rooming-house to another, then to a sheltering home, then to the roominghouse again.

(c) The patient had become litigous and querulous.

(d) The patient developed plans which

appeared to the social worker unrealistic and incongruous when compared with his social and economic setting.

(e) The patient seemed to play a social role which did not correspond to the actual surroundings but to the social goals and standards of his younger life period.

(f) The patient showed an undue degree of dependency. This manifested itself in frequent interviews with the social worker and in an apparent refusal to work when certain forms of employment were still open.

(g) The patient had marital difficulties.

Childhood Background—The description of an unfavourable childhood background, such as rejection, overt hostility against one parent, unfavourable orphan situation, bad marital background of the parents was given by 35 out of all patients. There was no correlation between this finding and any one single group. There was, however, a correlation between this finding and the marital status. There was an unexpectedly high incidence of unmarried persons among those who gave an unfavourable history of their childhood.

TABLE 5. MARITAL STATUS AMONG CASES WITH UNFAVOURABLE CHILDHOOD HISTORY

	Widowed	Married	Separated	Single
Marital status among total group	37	29	13	21
Marital status among cases with unfavourable childhood history	7	7	7	14

This finding is of statistical significance, the probability of chance occurrence being less than 1 per cent.

Rorschach Observations.—Rorschach records were obtained on 41 patients of 60 and more years of age. The findings are summarized, and the cases are presented in four groups. "Basic maladjustment" indicates cases in whom there had been signs of faulty adjustment in earlier life periods (19 cases out of the 41 who took the test). "Maladjustment in higher age" indicates those cases where no such indication was given in the history, and in whom we had reason to believe that the patient's maladjustment manifested itself only after the age of 50 (10 cases). The third group consisted of depressive patients who, at the same time, suffered from arterial hypertension. We chose these patients in order to probe for superimposed organic signs (7 cases). The fourth group is composed of psychotic patients who suffered from functional psychoses but lived in the community (5 cases). Here we present only a tabulation of the neurotic signs (Miale and Harrower-Erickson, 20), the organic signs (Piotrowski, 23), and an evaluation of the ratings of the instability vs. disability (Ross and Ross, 27).

TABLE 6. NEUROTIC SIGNS (MIALE AND HARROWER-ERICKSON, 20). AVERAGES FOR GROUPS

	Maladjustment Basic	Maladjustment Higher Age	Hypertensive	Psychotic
1) R less than 12	.47	.3	.28	.4
2) M not more than 1	.53	.2	.14	.8
3) FM twice M or no FM	.58	.4	.28	.6
4) Colour shock	.89	.4	.56	.8
5) Shading shock	.37	.2	.56	.2
6) Reject one or more cards	.27	.3	.42	.4
7) F greater than 50%	.37	.4	.28	.2
8) A greater than 50%, or A% + At% greater than 65%	.68	.6	.56	.2
9) No FC	.74	.8	.84	.6
Totals	4.9	3.6	4	4.2

It can be seen from a survey of these 41 cases that there is very little emphasis on the so-called organic signs. The so-called neurotic signs of Miale and Harrower-Erickson (20) are unspecific signs of emotional disturbance. These authors emphasize that at least five of these signs are needed to allow the suspicion of psychoneurosis on the basis of the Rorschach findings, and our cases do not reach this minimum. However, as a whole the tendency is more marked

TABLE 7. PIOTROWSKI ORGANIC SIGNS. AVERAGES FOR GROUPS

	Maladjustment Basic	Maladjustment Higher Age	Hypertensive	Psychotic
1) R less than 15	.64	.5	.71	.4
2) Time more than one minute		.1		.2
3) M not more than 1	.53	.2	.14	.8
4) F + % below 70	.1	.1	.14	.2
5) P% below 25	.27	.4	.14	.2
6) Cn	.05			.2
7) Repetition	.1	.1		
8) Impotence				
9) Perplexity				
10) Autonomic phrases	.05			
Totals	1.7	1.4	1.13	2

TABLE 8. INSTABILITY AND DISABILITY RATINGS

	Maladjustment Basic	Maladjustment Higher Age	Hypertensive	Psychotic
Instability	13.8	12.7	15.4	12.6
Disability	7.8	11.7	9.5	6.2

than that with reference to the organic signs of Piotrowski. This difference comes out even more clearly after the computation of the so-called instability vs. disability ratings by Ross and Ross (27). All this confirms what we have seen clinically, i.e., the cerebral impairment associated with aging is the least important factor which brings these clients to a psychiatric consultant.

DISCUSSION

The most pertinent facts arising from this survey are the following. In the faulty adjustment of people of the involutional and old age period organic cerebral decline plays the least important role. The most important factors are those of social and emotional adaptation. Moreover, it seems from this preliminary survey that during the late phase of life free anxiety as we encounter it in young and middle-aged adults, with its characteristic pattern of autonomic complaints, diminishes considerably. This makes further studies necessary in which the objective autonomic concomitants of anxiety are observed comparatively in different age groups. Moreover, phobic anxiety was seen only in one case, and compulsive-obsessive trends as well as hysterical conversion symptoms were inconspicuous within the entire group.

In order to evaluate these findings we must keep in mind that we have an almost uniform social and economic group under observation. There is no doubt that in a social agency which looks after the aged in the community we have to expect to find a high incidence of patients with character neurosis. Those who during the latter period of life are pushed by the current of social and economic maelstrom into a marginal position may find themselves there because of simple maladjustment in earlier periods of life. Hence there is a selective principle in our counselling setup. The final proof for this could be given only if we were able to have a similar counselling center for people of the middle and upper class. However, this is impossible to arrange, and patients of later maturity who are seen in private practice would not provide any adequate control because the very principle of selection is different. The same holds true with reference to normal people from all classes of the average population who volunteered to be examined by the questionnaire and interview method (Fried and Stern, 7).

A social and economic selective factor may also explain the absence of marked compulsive-obsessive trends within our group. The probability that a character with marked compulsive-obsessive trends may become indigent in the later life period is much smaller than in the case of a shiftless individual or a person whose main difficulties lie in interpersonal relationship. Nevertheless, in spite of the selective factors at work in our group we have to consider the possibility that floating anxiety diminishes with the decline of life.

If this is true it could be explained on various grounds. First, according to Freud (6) free anxiety is largely a product of repressed libido, and it is possible that, with the waning energy of the id, floating anxiety diminishes. At any rate, our clinical observations suggest that the autonomic expression of anxiety decreases in old age. It is a well-recognized fact that the age incidence of peptic ulcer reaches its peak around 35 years, and then decreases. Moreover, Friedman and Snape (9) have demonstrated in children that there is a characteristic change in the vascularity of the intestinal mucosa following psychic stimuli in cases of colostomy in which the mucosa can be inspected in vivo. It seems that this reaction decreases or disappears with advancing age (Friedman, 8). This, together with the pattern of complaints as observed in our patients, suggests a comparative study of the objective autonomic changes concomitant with anxiety in the old age group.

Another possibility to explain our observation is that the many objective fears of which the patient is conscious during this age period and of this particular social setting, act as absorbers for whatever free anxiety may exist. The patient is able to objectivate anxiety. This may be the reason why he does not complain of tremor, palpitation, sweating, increased peristalsis, or of an inability to enter a crowded room, but of worries or about his objective somatic illnesses. A similar mechanism may explain why hysterical conversion symptoms in the strict sense were not encountered in our group. Here, too, the objective physical handicaps act as absorbers, and whatever factor would produce conversion symptoms in young people may only accentuate the common psychosomatic mechanisms or produce hypochondriachal preoccupation. Moreover, in this social and age group, few secondary gains may be expected from acute symptoms of conversion hysteria. Thus, the present study indicates, if not a true diminution of anxiety itself, at least a characteristic shift in the pattern of symptoms.

Why is the bulk of our clients composed of those with problems in the field of interpersonal relationship? Goldschmidt (10) and Lewis and Goldschmidt (16) in recent studies emphasized the problem of lack of social integration in the later phase of life. They demonstrated that the separation of generations has gone far, and advised the living together of old and young people in larger households. Goldschmidt's detailed observations seem to underline the fact that industrialization and urbanization are responsible for the social problem of old age. In a rural type of civilization the old person has a greater chance to play a positive role. In industrial civilizations in which speed of of motor performance is decisive for the social value of the individual, a social devaluation and lack of social integration present the problem of the aged (Kardiner, 14).

What is not so apparent in Goldschmidt's studies is the question of the selective principle. Is the person who has difficulties in the field of interpersonal relationship throughout life apt to "show up" more in later maturity? First, we must keep in mind that to a person who has a tendency to social isolation the working unit is often the only group into which he is well integrated. The working harness provides, at the same time, a social corset, as it were. Once infirmity has removed this, the lack of social integration of the individual may become relatively prominent. Such a predisposing tendency may be surmised from the fact that we found in our cases a statistically significant correlation between unfavourable childhood background on one hand, and incidence of single marital status on the other.

There is another reason for this social maladaptation which has hitherto received little attention. Part of the consciousness of self is in reality a consciousness of what we appear in the eyes of others, the role we play in our social group. This, however, can go so far that the person identifies himself in his consciousness totally with his role. Allport (1) pointed out that even the very concept of personality was often influenced by,

or mistaken for, the social stimulus value (May, 19). If the person identifies himself with his social mask, his *moi superficiel* (Bergson, 3) or "persona" (Jung, 13) it is obvious that he will be subject to extreme maladjustment when he is culturally or socially displaced.

We saw this very markedly in the group investigated here. There was a type of client in which this mechanism appeared as the very nucleus of the problem. These were persons who, in their way of speaking and in their demeanour, behaved like puppets from a stage play of the Edwardian period. They were usually as fastidiously dressed as their circumstances permitted and emphasized a British accent. In the beginning we felt that this was nothing but the well-known phenomenon of genteel poverty. However, on studying these cases more carefully, it became obvious that we were dealing with a deeply-rooted maladjustment which had brought the patient into a helpless and dependent situation. It appeared that the patient, rather early during the process of identification, had adopted the social appearance of a parent—in other words, had identified himself with a parent's persona and had maintained this identification throughout life rigidly, against all demands of reality.

Miss P.R., 62 years old, lived in miserable quarters in a rooming-house district. She complained of lumbago and shortness of breath. However, a private physician who had followed her up for years felt that there was nothing organically wrong and that she was temperamental and eccentric. The social worker referring her added that the client seemed to have a very unrealistic attitude to the question of work, that she felt work was "not suitable for a lady" and that she undertook such things as voluntary work for the Red Cross although her main problem was that of destitution.

She was a woman of middle height, rather asthenic, with the typical asthenic profile. She looked approximately the stated age of 62. One could see that she must have been pretty in her day. She had apparently been waiting before the examiner arrived and she started the examination right away with a big flourish. She spoke slowly in a stilted Victorian English. She had a stammer, particularly noticeable when she pronounced words beginning with "m," but most of the time she was able to cover it up very nicely. It was noteworthy that her stammer was worst when she was asked about her menstrual history and also when she spoke about the janitor of the house (this last topic had strong implications of sex for her).

Her history, briefly given, is as follows:

She was born in 1884. Her father died of flu at the age of 44. At that time she was only two years old ("I was wee, wee, wee"). The mother remarried a "prominent man of science." The patient was then three. She described the stepfather in glowing colors. Her feelings about the mother, however, were mixed. "She was quick-tempered, high-strung and yet sweet at the same time."

When Miss R. was 27 years old her father received an appointment at a university in a comparatively small city. The mother took this very badly, obviously because of reasons of prestige. "To think—Kingston, and not Toronto!" The mother found it beneath her dignity to move to the smaller town. The father was very kind about it. He came home over weekends. However, the mother kept on grumbling—"I wonder what my husband is doing with all these pretty women around in Kingston?" At the same time the mother was afraid of aging. She was very nervous. She used to see flashes of light, and at the end she had a haemorrhage of the brain. Miss R. had to be around the mother constantly. She feels now that she ought not to have sacrificed all those years to her mother. "And all that time in that lovely home on ———street, with nurses, money and everything it can buy!"

She was 32 when her mother died. For another five years she had to humour her father when he came home. He suddenly had a stroke while lecturing in the amphitheater, and after six months in hospital, died. Miss R. indicates that the hospital took a good deal of his money. "After my father died I should have got rid of that big expensive home. That is where I made the blunder. I clung to these old fogey ideas. You know high-class people, how crazy they are sometimes." Not only did she retain the large home, but though she lived there entirely by herself, she kept a maid and butler as well. A trust company advised her against all this. Soon

she got into financial difficulties. "And all the time I was hiding this from my friends—I had a very calm exterior."

Her entire subsequent social history is characterized by the discrepancy between the social mask she kept on the one hand, and her actual economic state on the other. There were a few futile attempts to support herself by giving music lessons, but as a whole her financial dealings were characterized by complete impracticability. Five years ago she received $4,500 from a mortgage loan, which she invested unwisely on the ill-meant advice of some people who wished to take advantage of her. They advised her to buy "revenue-bringing property." She bought a house in the cheap rooming-house district but soon found that her original inspection of it had been framed. "It was a whorehouse—that was not for me—I purified the house. From then on it was no longer a good investment." All the time she had to have signs up "apartments to let." Four years ago she had to sell it again for $1,500 to its former owner.

Many debts had accumulated and she had to sell many of her possessions, including her piano (although she used to give music lessons occasionally), her radio, etc. "I always kept up a bluff, and in the evening I shovelled coal." She is now living on support from the Family Welfare Association.

She says that she used to have many friends. She emphasizes that they were always "clean." "I have always been firm, naturally, we all are made of flesh." She describes particularly a friendship with a man which she kept for eight years. He was a "clean-living man." "Remember, it was a clean friendship." He admired her greatly. Suddenly she got a letter that he had married. This was quite a shock, but she wrote back to him "I hope you will be happy."

She had learned to play the piano as a child and at the age of eighteen she was accomplished enough to become a piano teacher. She used to teach off and on until she had to sell the piano four years ago. "Whenever things were bad I put my music to good use." Apart from this she would give lessons in French (she is entirely bilingual). It seems that she also made a little money through some business transactions but most of the time she seems to have been very badly "clipped."

Throughout all the interviews she appeared with a peculiar shabby elegance, wearing evening-length gloves, and there was about her a faint odour of old lavender.

It was obvious from her history that she had a very ambivalent attitude towards her mother, and as is so often the case in marked Oedipus situations, she had adopted some of the traits of the mother which she consciously rejected most. The mother had apparently been unable to detach herself from thinking in certain social categories of the late Victorian period. Miss R. has adopted this and never made any practical social adjustment. Thus she had a peculiar mixture of a Victorian mask ("persona") and a good sense of reality. She maintained a large house with a butler and a maid at a time when this was entirely out of proportion, and she clung to a false appearance for the greater part of her life. This incongruity became more pronounced by the mere passing of time, so that it formed the chief problem of her later life period.

Mr. E.F. was born in 1889 in New York. He belonged by descendence to three prominent wealthy families. His father was a celebrated surgeon. His mother was a writer and poet and was active in politics and welfare work. His sister was also a writer and prominent in politics. His maternal grandmother was Lady G———. The social workers were always impressed by the way in which he basked in the reflected glory and prestige of his family, and this was the favorite theme of his conversation.

He first applied to the Family Welfare for aid in November, 1944. He was destitute. His winter clothing was in pawn, and he appeared physically over-wrought and on the verge of a breakdown.

When he was seen by the counsellor for the first time, in September, 1945, he appeared as a gentle, soft-spoken man with an affable manner. His clothes were clean but apparently old. He sported a pince-nez on a black string, and his behaviour was that of the Edwardian drawing-room. He had a considerable stammer. He dwelt unduly on unimportant details of the past, particularly on things pertaining to his family, and more than anything else, his mother. He produced spontaneously family photographs, newspaper clippings of obituaries, printed poems written by his mother, numerous sentimental knickknacks. The manner in which he presented his history was characteristic of a type of elderly bachelor encountered in our group. There was

a very strong mother fixation, "mother" comprising not only the actual person but an entire social and cultural setting of a past generation. This, the complete submission to the father in the Oedipus situation, was so strong that the client, who was rather delicate, passive and submissive by nature, had never made an aggressive and realistic approach towards life. When speaking of the now famous persons who used to go in and out of his father's house he showed neither envy nor resentment. In fact, during all the spontaneous conversations during the interviews he never touched on the sore points of his life or the blows he had received. He went to see cabinet ministers who had been friends of his family when he was young but his plans were always high-flown and unrealistic.

He was obviously pained to have to wait with other clients in the waiting-room of the social agency. When the counsellor on one occasion gave a public lecture the client attended it and afterwards sent him a letter of acknowledgment which, in its general layout and in its style, could have come from a prime minister.

We see that these patients assimilate accidental cultural patterns into their behaviour, and therefore show an extreme example of "displacement in time" which is one of the mechanisms of maladjustment *specific* of the higher age group.

This mechanism deserves further study. It is interesting to see that in some of these clients it was impossible to penetrate the mask. In other cases insight could be obtained into the unrealistic attitude. The lady described above came to understand the mechanism of her faulty attitude to an astonishing degree, and after several interviews took up nursing as an untrained attendant.

Old age counselling affords the unique opportunity of studying the development of personalities in full longitudinal sections. When we first began to survey the total number of our clients we purposely adopted, among other categories, those used by Grinker and Spiegel (11). We felt at that time that the reaction of people stranded during later maturity is, in its mechanism, comparable to operational fatigue following combat. We saw, however, that certain reactions, such as free anxiety with its autonomic manifestations, phobias, and conversion hysteria are much less significant than they are in young people following acute stress. This suggests that the mechanisms of defense and of flight change characteristically. The chief differences are (a) that stress and danger of the struggle for existence is prolonged and never as acute as in military combat, (b) that in old people the awareness of reversibility of the life situation diminishes characteristically (Schultz, 28), and (c) that the somatic apparatus which reacts has undergone a change. Apart from this there is, of course, as was pointed out previously, a selective principle at work in our particular group.

The present study suggests that the position of the aged in the community is a problem which has never been approached adequately. One of the first aims of all social and clinical studies should be to bring on a fundamental reorientation in the field of legislation and social action.

Summary

An Old Age Counselling Center was established in association with a social agency. Since it was advisable to study the problems of old age in conjunction with those of involution, the lower age limit of patients was set at 50 years. The present study gives a preliminary survey of our findings in the first 100 cases. Aging in the sense of organic cerebral decline plays the least important role in such a group. There is evidence to indicate that free floating anxiety with the common autonomic symptoms diminishes with old age. In the present group simple maladjustment was most prominent. Phobic anxiety was almost absent. Conversion hysteria and compulsive-obsessive states were absent. The absence of the latter may be explained on the basis of a selective factor. The prominence of simple maladjustment may also be explained on the basis of a selective factor, but in addition there are specific features in the position of the aged in society which tend to stress pre-existing

faults in the social integration of the individual.

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Submitted for publication August 18, 1947

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CURRENT COMMENT

Fear Begins at Forty

A vivid dramatization of a problem confronting many American families today was presented by the Columbia Broadcasting Company Documentary Unit on October 28, 1947.

It is in 1939 that Pa, a capable, industrious worker loses his job—merely because he is 60 years old. One day he is wanted; the next day he is not, although he knows the paper-box business thoroughly and has been with the company 29 years. In spite of all his efforts, he can find no work because of his age. There is nothing for Eddie and Flo, the son and daughter-in-law, to do but take Pa and Ma into their four-room apartment with them and their own two children.

Conflicts because of habits and differences of opinion in disciplining the children are inevitable with any six people of three generations living in so small a place, but somehow they manage. Then comes Pearl Harbor and the company begs Pa to take his old job back. Pa is proud to do his part in winning the war, and he does it well. He and Ma take their old apartment back . . . life is again running smoothly. But when the cheering of the winning the war dies down, Pa is given his honorable discharge. One day he is a valuable employee, given a reward for efficiency and production ideas, and a few days later he is useless again, an old man.

Again Pa can find no work because of his age; he is now 65. And Ma needs medical care. She calls the Welfare Agency about entering a home and finds that not only do the homes have long waiting lists, but also she and Pa would have to be separated. Eddie, too, takes the problem to the Social Welfare Bureau. They are sympathetic but they too can offer no help. Pa and Ma could enter an institution if there were money to pay for their care; if the home had a vacancy; if there were nothing else Eddie could do for them.

There isn't. Eddie visits a few of the homes and is hopelessly discouraged. There is no acceptable solution to the problem. Then Eddie hears Pa's voice. He has perfected an invention which has made him wealthy. But it is only a dream. And reality forces Eddie to rent a shabbily furnished room for his father and to place his mother in a home where he hopes she will get the medical care she needs.

Fear is brought home to Eddie, too. He is no longer young, and he fears the day when he and Flo will present the same problem to their children. Eddie talks it over with a geriatrist, an employer, a sociologist, a member of the Welfare Board, a social service worker . . . each presents his views on the subject and his hopes of what can be done. Eddie reiterates the theme of the program—unless something is done, unless

The establishment of the JOURNAL OF GERONTOLOGY has been made possible by a grant from the Josiah Macy, Jr. Foundation in support of the editorial office.

The hieroglyphics, "The Beginning of the Book for Transforming an Old Man into a Youth," at the top of this editorial page, are from the Edwin Smith Surgical Papyrus, translated by Professor John Breasted, University of Chicago Press.

everyone supports the many things that can be done, there is nothing ahead but the fear that begins at forty.

Columbia Broadcasting Company is to be congratulated on their courage in presenting this important problem to the people of America.

Compulsory Retirement

In an address in October to the New Haven Medical Society and again in December to the New York State Joint Legislative Committee on Problems of the Aging, Dr. Theodore G. Klumpp pointed out that "Compulsory retirement by 1980 of all workers 45 years of age or older" was foreseen if the present archaic system of retiring workers solely on the basis of calendar age is maintained.

The more workers we retire, the more we lower the calendar age, the greater will be the economic burden on those who continue to work. Dr. Klumpp predicted the introduction of a 30-hour week in industry within a generation.

The following recommendations were proposed:

1) Compulsory retirement on a calendar age basis be abandoned since physiologic age is not the same as chronologic age.

2) Retirement, like hiring, be selective and based on fitness to do a given job.

3) Compulsory retirement be based on the recommendation of a retirement board composed of medical and psychiatric members as well as administrative officials.

4) Opportunities for down grading in position and salary be offered the aging worker, just as the young apprentice works himself up in skill.

5) Industry, governmental, and private institutions make a greater effort to employ partially disabled persons.

6) Institutions for the aged and disabled be changed from asylums to modern institutions where every convenience and scientific development is available for their physical, mental, and spiritual comfort.

In the same vein, Ewan Clague, Commissioner of the Bureau of Labor Statistics, indicates that a large number of workers in their forties, workers who expect to work until they are 65, are being forced out of their jobs and that it will not take even a major depression to bring the problem to a head. He feels that the choice will have to be made between lowering the present 65-year retirement age under the Social Security System to remove older workers from the labor market, and taking steps to assure the continued usefulness of the older employee as a productive worker.

City for the Aged

The appointment of a National Advisory Council for Research in gerontology for the fraternity's city for the aged at Moosehaven (near Jacksonville), Florida, has been announced by the Executive Director of the Loyal Order of Moose, Malcolm R. Giles. Their first meeting will be held in February and definite research plans will be made at that time.

The members of the Council are:

Dr. Allan G. Brodie, Dean, University of Illinois, College of Dentistry, Chicago (Anatomy and Orthodontia).

Dr. Anton J. Carlson, Emeritus Professor, Department of Physiology, The University of Chicago (Physiology).

Mr. Louis J. Haas, Director, Men's Therapeutic Occupations, New York Hospital, White Plains, N.Y. (Occupational Therapy).

Dr. George Lawton, Consulting Psychologist, New York City (General Gerontology).

Dr. S. L. Pressey, President, Division on Maturity and Old Age, American Psychological Association, Ohio State University (Psychology of Aging).

Dr. Martin L. Reymert, Director, The Mooseheart Laboratory for Child Research (Psychology).

Dr. N. W. Shock, Chief, Gerontology Section, Baltimore City Hospitals (General Gerontology).

The Loyal Order of Moose established the well-known Mooseheart Laboratory for Child Research seventeen years ago at their City of Childhood, Mooseheart, Illinois, a city of about 1000 normal children, ranging

in age from birth to 19. The facilities of this laboratory and child city for research in human development have been utilized by national scientific bodies, universities, and individual scientists. The Fraternity now extends its support of research to the old age group and hopes to make Moosehaven a model for the country in the care of the aged, and also to establish there a department of research available to all. Inquiries from interested scientists may be addressed to Dr. Martin L. Reymert, Mooseheart, Ill.

Syndicated Columns on Aging

More and more attention is being paid to the problems of the elderly in the nation's syndicated columns. Elsie Robinson writes that adaptability is the true test of one's age; Bob Thomas states that most big male movie stars are over 40; Harold Heffernan, too, believes that the screen's "he-lovers" are growing older, Dr. William Brady devotes a column to how long it takes to grow old, and Helen Straus explains that today there is a larger number of mothers over 35. And Dr. Paul Popenoe produces three articles, one on the need of old folks for a social life of their own, one to the effect that old folks are still human beings and have the same mental and emotional needs as young people, and one on how to keep busy when you retire from your job.

More About Recreation Projects

The Philadelphia Recreation Association has produced a pamphlet by Joseph Dietch, "Something to Live for—and Sing About" which details in narrative form the splendid work that Philadelphia is doing to help their elderly to combat idleness, to give them an interest in life.

Fun After 60 Hobby Show, under the auspices of the Community Project for the Aged, Council of Social Agencies, Wieboldt Foundation, was held in Chicago from November 18 through 23 with the following commendable aims:

"To exhibit articles which display the talents, workmanship, abilities, and interests of the older person.

"To demonstrate that as long as a person lives he can be productive and useful.

"To give the older person a chance to show and share his interests and hobbies and have a good time doing it."

New York Initiates Two Committees on the Problems of Aging

The New York State Joint Legislative Committee on Problems of the Aging met on December 11, 1947. Members of the Advisory Committee on Longevity, the Advisory Committee on Employment Problems of the Elderly, and the Advisory Committee on Recreation for the Elderly were listed and a comprehensive program covering many of the problems of the elderly was presented by well-qualified speakers.

The Department of Health of New York City under Commissioner Harry S. Mustard has appointed an Advisory Committee on Geriatrics with twelve members and Dr. C. Ward Crampton as Chairman. On December 19 the committee held a meeting and conducted a preliminary discussion concerning various ways in which the Department of Health might become more active in the field of geriatrics.

British Medical Society for the Care of the Elderly

The British Medical Society for the Care of the Elderly was formed on September 26, 1947, at St. John's Hospital, Battersea, with membership open to all medical practitioners who are interested in the care of the elderly. Dr. Trevor H. Howell is Honorary Secretary, Dr. Thomas S. Wilson Honorary Treasurer. It is proposed to hold clinical meetings from time to time in various hos-

pitals so that members may have an opportunity to discuss the social and medical aspects of the care of the elderly patient.

The following are the aims of the Society:

1. To improve the standard of medical care among elderly patients.

2. To coordinate the activities of those concerned with the care of the aged and chronic sick.

3. To cooperate with other bodies interested in the social and medical problems of old age.

4. To promote the exchange of ideas and opinions on the clinical and administrative aspects of geriatric medicine.

5. To encourage investigation and research in the diseases of old age.

The formation of this new society is evidence of the increasing interest in this field. The JOURNAL OF GERONTOLOGY wishes the new society every success.

Elders in the News

Francis Saiz, Navajo Indian reputed to be 137 years old, died in San Patricion, New Mexico, January 21. Another of the nation's oldest citizens, "Aunt Martha" Payne, Negro, died in her home in Lynchburg, Virginia, November 22. Her age was estimated at between 125 and 127.

* * *

Mrs. Mary Gerrow, Schofield, Wisconsin, who was 103 years old Christmas Day, hoped someone would invite her for an air ride; she hasn't been up since she was 95.

* * *

Mrs. John Slazyk of Avoca, Pennsylvania, a spry little woman of 103, celebrated her birthday October 15 by walking four miles through the woods in search of mushrooms, gathered four buckets of coal, worked in her garden, and fed her flock of fifty chickens.

* * *

William Kowazek, one of Missouri's few surviving Civil War veterans, celebrated his one hundredth birthday. He donned his uniform to have his picture taken and went for a short walk.

Mrs. Isabelle Wilson, Pittsburgh, Pennsylvania, celebrated her 102nd birthday by eating a birthday dinner and cake cooked for her by her son, Charles, 80.

* * *

Pride and courage were shown by Mrs. Muriel Salisbury, 101, a widow, childless, and broke, when she was ordered out of her apartment. "I can still work," she said.

* * *

William Borders, St. Louis, who will be 100 on April 1, said, "I'm tickled to death to be living." * * *

Jake Ambrose, who at 96 is the oldest man in Calhoun County, Illinois, and Mrs. Mary Becker, 79, were married in December. It was the sixth marriage for Ambrose and the second for Mrs. Becker. All of the marriages were dissolved by death.

* * *

Mr. and Mrs. Thomas Rose, Whitney, Texas, renewed the marriage vows they first exchanged 75 years ago. He is 95; she is 93.

* * *

Runner-up on the claim of one of the oldest marriages in the nation is that of Joseph and Sarah Arnold, Salem, Illinois. They observed their seventy-second anniversary in October. Arnold, who will be 90 in February, still gardens and helps with home chores, and Mrs. Arnold, 86, continues to "run" her home. * * *

George B. Knight, 95, claims that when he voted in the latest Mississippi Democratic primary it marked the seventy-fourth consecutive year he has voted in every political race in Jones County. He said he had never failed to vote since reaching 21, and has always voted with the winning side.

* * *

Mrs. Mary Gallagher, 91-year-old Irish woman, flew the Atlantic to spend the rest of her days with her children.

* * *

Bion L. Burdick, 90, of Petersburg, New York, renewed his New York state automobile driver's license.

* * *

General of the Armies, John J. Pershing, observed his eighty-seventh birthday Sep-

tember 13 at the Army's Walter Reed General Hospital.

* * *

Themistocles Sophoulis, Prime Minister of Greece, is 85, 87, or 89 years old, depending on who is telling it. "Me old?" he has said, "My father lived to be 105, and I'm in better shape at my age than he was."

* * *

An 84-year-old son of Italian immigrant parents who quit grammar school to earn a living selling fruit, has given a fund, ultimately amounting to $3,000,000, to the Boston public library, where spare-time reading helped him make a fortune.

* * *

Coming out of a retirement which started in 1946, 78-year-old Thomas Moses of Danville, Illinois, still has the necessary drive to head Illinois' mines and minerals department.

* * *

Mrs. Tessa McLeon, of Boulder, Colorado, at the age of 72 plays golf every day she can, prefers an 18-hole game which calls for players with stamina like herself and not the nine holes which she considers primarily for the younger set.

News and Notes

A meeting of the Club for Research on Aging was held in New York on February 9 and 10.

A trust fund of about $1,410,000 was bequeathed to the Washington University School of Medicine for research in geriatrics and allied fields. No definite plans for the program have been formulated as yet.

The Pharmaceutical-Medical Research Foundation was established by the American Pharmaceutical Manufacturers' Association and the American Medical Association in December for basic medical research to improve human health and prolong useful life. Initial work will deal with the degenerative diseases of old age. The Foundation is expected to have a first year fund of $225,000, and a total expenditure of at least $1,250,000 was planned in the first five years.

The two group therapy series for adult men and women of the middle years and older conducted by Dr. George Lawton in December will be repeated in March and again in May. Each series will run for ten meetings with discussions lasting about seventy-five minutes and will be held in Dr. Lawton's office, 41 West 82nd Street, New York 24, New York.

The British Society for Research on Ageing, Oxford, England, has published a list of members of European and American Societies for Research on Ageing.

The National Association for the Employment of the Handicapped, a voluntary organization, was recently organized and incorporated with its office at 1026 Seventeenth Street, N.W., Washington, D.C. It is taking over the work that was done by the Retraining and Reemployment Administration, Department of Labor, in the last two years in promoting the employment of handicapped people. The scope has been broadened to include mentally as well as physically handicapped persons.

The National Society for Medical Research, organized in 1946 and with headquarters at 25 East Washington Street, Chicago 2, Illinois, advocates among scientists an acceptance of responsibility for public understanding in the various fields of knowledge, attempts to aid those who contribute to public education, and directly opposes the antivivisection cult.

In addition to editorial material placed in this section the JOURNAL OF GERONTOLOGY will accept notices of positions open.

GLUCOSE TOLERANCE IN THE AGED

The effects of advancing age on different metabolic functions are little understood, although their importance is widely recognized. One area in which a number of studies have been reported is that of carbohydrate metabolism in the aged .

The glucose tolerance test is one important index of the status of the carbohydrate metabolism in an organism. This test determines in essence the rate at which added glucose is removed from the blood stream. The amount of glucose in the blood may be increased either by feeding sugar or by injecting it directly into the blood stream.

The oral test is performed on the patient in the morning under basal conditions (at least twelve to fourteen hours without food). A fasting blood specimen is drawn by venipuncture, and then 80 to 100 gm. of dextrose in 250 cc. of cold water are ingested. Blood samples are drawn at 30, 60, 90, 120, and 150 minutes. The normal type of curve obtained by this method has been described by Mosenthal (New York State Journal of Medicine, *46:* 2513-2518, 1946) as follows: Fasting level 120 mg. per cent or less with a rise within 30 to 60 minutes to 180 mg. per cent or less and a subsequent fall to 120 mg. per cent or less within two hours.

Any curve which does not follow these criteria is abnormal. The abnormal types of curves may be divided into a number of different classes; broadly speaking all curves may be classified as either "flat" or "diabetic." The flat type is a curve which does not rise above 150 mg. per cent within two hours. This poor response may indicate poor absorption of the glucose from the gut. The diabetic type of curve is one in which the highest blood sugar value is above the normal range (190 mg. per cent), and the two and a half hour value has not returned to fasting level. This type of curve, although called the diabetic type of curve, does not necessarily mean the subject has diabetes but simply means the patient's homeostatic mechanisms for maintaining blood glucose levels are disturbed. Other symptoms must be observed before the clinical diagnosis of diabetes can be made.

The second type of glucose tolerance test, the intravenous type, is performed on patients in basal condition as previously described. The fasting blood sugar is drawn, and then 50 cc. of 50 per cent glucose is injected into a vein within two minutes. Blood specimens are drawn at 5, 15, 30, 60, 90, and 120 minutes after the beginning of the injection. In this type of test the maximum glucose concentration is observed at five minutes. The curve then falls rather rapidly and reaches fasting levels within two hours (Lozner, Winkler, Taylor, and Peters, Journal of Clinical Investigation: *20:* 507-515, 1941). In this type of curve the peak value is of no significance, and only the time required to establish normal blood levels is considered. In classifying intravenous tolerance curves, the flat type is, of course, eliminated, since the factor of absorption from the gut is absent. Slow return to normal blood glucose values results in the diabetic type of curve and is interpreted as showing a decreased tolerance to glucose.

In 1926 Hale-White and Payne (Quarterly Journal of Medicine, *19:* 393-410, 1926) performed oral glucose tolerance tests on old people and reported that the peak of the curve was higher and the decline slower than normal.

Since then similar results have been reported by other investigators, and the general opinion is that there is a decreased tolerance in old people after the ingestion of glucose. The peak of the oral glucose tolerance curve observed is higher, and the decline is much slower than normal (Hofstatter, Sonnenberg, and Kountz, Biological Symposia, 11: 87-95, 1945; Aaltonen, Acta medica Scandinavica: *99:* 356-386, 1939; and Romeke. Acta medica Scandinavica, Supplement 39, 1-50, 1931).

This decreased glucose tolerance in the elderly has been attributed to various mechanisms. First, it has been thought that in old age the capacity of the isles of Langerhans of the pancrease to produce insulin is decreased. In a review of the literature, Shock (Kaplan, Mental Disorders in Later Life; Chapter 3, 7-23, Stanford University Press, 1945) doubts this, giving as his argument the fact that the incidence of diabetes drops off sharply between 50 to 60 years of age; whereas, if there were a decreased pancreatic response in old people, one would expect the incidence of diabetes to rise progressively with age.

Other evidence against the poor pancreatic response theory are the experiments of Soskin and Allweiss (American Journal of Physiology, *110:* 4-7, 1934). These authors, using depancreatized dogs, gave a constant glucose infusion with just enough insulin to maintain a constant blood sugar level. When glucose tolerance tests were performed on these dogs a normal type of curve was obtained without increasing the rate of infusion of insulin. This work indicates that it is not necessary to have stimulation of the pancreas with increased insulin secretion to obtain a normal glucose tolerance curve.

Even if there is a decreased insulin content of the pancreas in old age it is not necessarily because of old age itself. Blotner (Archives of Internal Medicine, *75:* 1-6, 1945) has shown that physical inactivity results in a lowered glucose tolerance. Since lowered physical activity is often present in the elderly, this factor itself may be the cause of lowered glucose tolerance.

Since the curve obtained after the oral ingestion of glucose is the resultant of two factors, namely absorption and utilization, abnormalities of the curve may be because of abnormalities in either factor. Because of this some investigators have attributed the delayed fall of the blood sugar to faulty absorption in old people. That absorption does vary considerably has been shown by repeated oral glucose tolerance tests. Of 43 patients who had repeated oral glucose tolerance tests, 25 (60 per cent) had a different type of curve on the second test (Lennox, Archives of Neurology & Psychiatry, *18:* 395-412, 1927). Also, John (Journal of Pediatrics, *14:* 737-744, 1939) revealed a fairly large variation in repeated oral tests on children. Freeman, Looney, and Hoskins (Journal of Clinical Endocrinology, *2:* 431-434, 1942) repeated oral tests on 35 patients and found a wide degree of variation.

Recently Horvath, Wisotsky, and Corwin (Journal of Gerontology, *2:* 25-30, 1947) performed repeat oral tests on 12 patients between 60 and 70 years of age. They divided the curves into four different types: I—Normal; II—Storage (curve in which maximum rise of 210 mg. per cent occurs within two hours and a delayed return to basal); III—Flat; and IV—Diabetic (author uses 240 mg. per cent as minimum value for peak of diabetic curve). The results revealed a wide variation in repeated tests. For example, on one patient 67 years old they made 11 consecutive tests, 18 days apart, and obtained the following types of curves: III, III, IV, I, I, IV, III, I, III, and IV respectively.

Thus it can be seen that it is difficult to ascertain the status of a patient's tolerance to glucose by a single oral test, since the reliability of repeated tests is very poor. If

faulty absorption is the cause of this, then the curve after the intravenous injection of glucose should be normal. Lozner, Winkler, Taylor, and Peters (Journal of Clinical Investigation, *20:* 507-515, 1941) performed intravenous glucose tolerance tests on 60 normal adults. They studied 14 patients 50 years of age or over in their series. They found no differences which could be attributed to age or sex. All of their patients had normal blood sugar levels at the end of two hours.

Another approach to the factor of absorption has been the comparison of oral and intravenous tests on the same subjects. Lennox and Bellinger (Archives of Internal Medicine, *40:* 182-194, 1927) performed 175 oral and 150 intravenous glucose tolerance tests on 100 subjects. They correlated values of an arbitrary index, designed to measure the proportionality of the peaks of the oral and intravenous glucose curves on the same subject. They found agreement between the two types of tests on the same subject in 75 per cent of their cases.

These results are open to several criticisms. The index they used is calculated by adding the highest value and the two-hour value of the curve and dividing the sum by twice the fasting level. They used the thirty-minute value as the peak in the intravenous test. A close correlation between the values of the index obtained on two tests would be observed only if the fasting level and the two-hour level were equal, or if the ratio of the fasting level to the two-hour level were constant. Often this is not the case. The authors also state: "Measurements of patients on whom repeated tests were made were more scattered than measurements of those on whom but a single test was made, probably owing to the fact that tests were repeated more frequently on patients who presented abnormal results." This, too, does not necessarily follow.

Gildea, McLean, and Man (Archives of Neurology & Psychiatry, *49:* 852-859, 1943) made oral and intravenous tests on 19 patients with manic depressive psychosis. Only 4 of their patients were over 50 years of age. Three of the 4 had prolonged oral recovery curves and 2 of these 3 had normal recovery curves on the intravenous tests. One of the 4 had a flat oral curve and a normal intravenous curve. In these few cases the prolonged oral curves seem mainly to be because of faulty absorption. However, these results should not be accepted too quickly in view of the poor reliability of oral glucose tolerance tests.

The reliability of the intravenous tests has not been extensively studied. Lennox (Archives of Neurology and Psychiatry, *18:* 395-412, 1927) repeated both oral and intravenous tests on patients with epilepsy and on a few normal patients. These show considerable variability both in actual values and in the type of curve obtained on repeated intravenous tests.

Also Tunbridge and Allibone (Quarterly Journal of Medicine, *9:* 11-35, 1940) made repeated intravenous curves on the same subjects. They present only two graphs, both of which show moderate variation. Here again the actual values are not given.

McKean, Meyer, and Von der Heide (American Journal of Medical Sciences, *189:* 702-714, 1935) made 29 repeated intravenous tests and gave a frequency distribution chart for coincident points which revealed considerable variation. These authors used a different method in performing the test which is not without criticism. Their method consisted of injecting glucose intravenously over a period of one and a half minutes; then taking samples at three to five minutes for the peak, and samples at ten and fifteen minutes, completing the test at that time. They claim that one can tell as much about the patients' glucose tolerance from this brief curve as from the usual curve. They place the most importance on the peak of the curve and the fifteen minute sample. Results from this procedure are difficult to interpret.

It is a well-known fact that for the first three to five minutes after injection of glucose the level of glucose in the blood changes

rapidly and that the main factors influencing the level at this time are mixing and diffusion rather than utilization (Tunbridge and Allibone, Quarterly Journal of Medicine, *9:* 11-35, 1940). In fact, Greville (Nature, *150:* 522, 1942) used this as a rough determination of the water content of extracellular fluid and the red blood cells. Also there is an increase in blood volume during the first three to six minutes, because of the osmotic action of the hypertonic glucose, which may produce a 5 to 10 per cent drop in hemoglobin, according to McKean, Meyer, and Von der Heide (American Journal of Medical Sciences, *189:* 702-714, 1935).

Winkler, Taylor, and Peters (Journal of Clinical Investigation, *20:* 507-515, 1941), using a standard dose of glucose and standard injection time, found no relationship between the peak of the curve at five minutes and the remainder of the curve. Hence, it would seem that the peak of the curve is of no diagnostic value in the intravenous test.

The use of the fifteen minute level as the other point of evaluation is also of questionable value.

The distribution of the blood levels of the normal and diabetic patients at fifteen minutes lie so close together that although they are not overlapping, they are within the range of variability of repeat tests as reported by the author himself. Hence, the dividing level of 125 mg. per cent seems too arbitrary.

Many investigators have used only one or two points on the glucose tolerance curve as an index to the status of the patient's carbohydrate metabolism. The reason for this seems to be that one forgets just what the glucose tolerance test measures. The glucose tolerance test is essentially a stress test in which the rate of recovery to an induced hyperglycemia is measured. Since it is a measure of the rate of recovery, it is evident that an index which takes into account all the points on the curve would give more information as to the patient's ability to respond to the stress applied than just one or two points on the curve.

Greville (Biochemical Journal, *37:* 17-24, 1943) has equated mathematically the intravenous glucose tolerance curve with fair results. Before definite statements concerning glucose tolerance in old age or in many other conditions can be made, more investigation similar to Greville's needs to be done. This is particularly true in establishing the reliability of both intravenous and oral tests.

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THE CHOLESTEROL CONTENT OF DIETS FOR THE AGED

Cholesterol plays many roles in life processes in youth and age, but it has a menacing association with senility and the diseases associated with aging. Timothy Leary (Archives of Pathology, *32:* 507-555, 1941) among others, has suggested that arteriosclerosis may be related to the cholesterol content of the circulating fluids and tissues.

Cholesterol is confined to the animal kingdom and found only in products of animal origin. Animal sterols can be synthesized in the body. It is impossible to distinguish the source of any given molecule of cholesterol in the gastrointestinal tract since animal sterols are poured into the intestine in the bile and appear to be excreted or secreted by the intestinal mucosa. Cholesterol absorption, synthesis, and destruction are accurately attuned, and in normal individuals the totals show the documented accuracy of a C.P.A. audit.

Plant sterols are not absorbed as are animal sterols. Absorption of sterols involves highly specific chemical reactions. Peters and Van Slyke (Quantitative Clinical Chemistry: Interpretations, Vol. I, 1946, 387-389) give a chemical explanation of this discriminate absorption and state that minute differ-

ences of configuration may lead to rejection of a sterol. This is the case of allocholesterol and dihydrocholesterol, in which the isomers of cholesterol and the saturated form of cholesterol, respectively, are almost or completely excreted in the fecal matter. Okey (Journal of the American Dietetic Association, *21:* 341-344, 1945) states, "published figures for 'cholesterol content' of food of vegetable origin represent not content of cholesterol itself, but content of other sterols that have digitonids of similar solubility or that give similar color reactions."

Cholesterol is synthesized within the body, and the rate of synthesis bears some relationship to the amount which is absorbed. However, in the words of Dr. C. Ward Crampton (Final Report of the New York State Joint Legislative Committee on Nutrition, 1947, Meals for Millions, p. 124) "Blood cholesterol varies with health, illness, food and circumstances. Cholesterol, the 'liver sterol,' is one of the tetracyclic carbon group, like other sterols and sterones of this distinguished family. 'Tetracyclic' means it has a nucleus of four carbon group rings linked together with atoms of carbon, hydrogen and oxygen attached to the free corners in singles and in groups."

Authorities differ in opinion as to the lower and upper limit of the blood level of cholesterol but most give a difference in range of 60 to 80 mg. per cent (140 to 200 mg. per 100 cc. or 150 lowest limit and 250 highest limit in the zone). The suggested intake of total food cholesterol is approximately 100 to 200 mg. per day or less; hence foods contributing animal fat are limited in hypercholesteremia. The diet in arteriosclerosis obliterans is low in cholesterol, animal fat, and in associated obesity, total fat.

Cholesterol and its esters are associated with lipids in natural sources. The most important of the zöosterols is cholesterol. Cholesterol occurs in the lipid fraction of all organs, especially the brain and spinal cord, and in gallstones. It is found in every living cell and it is thought to serve as a protective agent for nervous tissue. In children with hypothyroidism the cholesterol level of the blood is elevated. Cholesterol levels of the blood in children are also correlated with bone age. It is probable that cholesterol may be the parent of the acids of bile and sex hormones. The adrenal glands are abundant in cholesterol, and possibly the product desoxycortico-sterone may develop from cholesterol. The exact nature of the manufacture of such cholesterol derivatives is not clear.

When Schönheimer and Breusch (Virchows Archiv für pathologische Anatomie und Physiologie und für klinische Medizin, *249:* 1, 1924; The Dynamic State of Body Constituents, Harvard University Press, Cambridge, 1942; Journal of Biological Chemistry, *103:* 439, 1933) gave rabbits large amounts of plant sterols (sitosterols and phytosterols) in plant tissue and vegetable oils the total sterols in their bodies did not increase. When only minute amounts of cholesterol were given the results were noted upon analysis. When a mixture of plant fat and animal fat was given, the pure cholesterol from the animal fat was recovered from thoracic duct lymph. Cholesterol is esterified by pancreatic cholesterase. The esters are then absorbed. Preformed esters may be hydrolyzed in the intestinal tract. These products are increased in deranged cholesterol metabolism. Here increased fat intake or increased concentration of bile salts in the intestinal tract makes for increases in cholesterol absorption. (The reader is directed to a further discussion of this in Handbook of Nutrition, American Medical Association, 1943, 35-48.)

Obvious sources of cholesterol are brains and egg yolk. While all animal fats as found in butter, cream, whole milk, cheese, and fatty meats contribute to the total cholesterol, the elimination of a few obvious sources will decrease the cholesterol level the most readily. Brains and egg yolk contain more than 1 per cent cholesterol; egg yolk (about 35 gm.) has one-third gm. cholesterol. Protein-rich foods which can displace animal foods rich in cholesterol are: lean meats of

non-glandular origin; lean fish, canned in plant oils or fresh; dry style cottage cheese also called Hoop or Farmer's pot cheese; soybeans, soya cheese or curd, soyflour or grits; seedmeal flours, cotton seed, sunflower seed, sesame seed; peanut granules and defatted peanut flour; legumes and legume flours; nuts, nut butter and defatted nut flours; non-fat milk solids, dried whey powder, edible casein; dried brewer's yeast; corn germ, partially defatted; wheat germ, partially defatted; egg whites; buttermilk or skim milk or reconstituted or filled milk in which the butter fat is removed and plant fats are substituted.

While no conclusive experimental evidence is at hand, some experiments point to a general direction in reducing the number of foods carrying cholesterol. When college girls were fed four eggs daily for a period of almost a month, the rate at which cholesterol was absorbed increased. More of the total cholesterol present was absorbed as the time went on. This would point us to the use of a mixed, varied, and alternating diet in which obvious sources of animal fat are decreased or spaced with larger concentrations of plant fats. Many menus tend to be a thoughtless drill and a repetitious routine and such menus could well afford to use some of the equally valuable plant fats instead of the commonly thought of animal fats. Instead of butter one might choose avocado, olives, sesame seed oil, soybean oil, olive oil, and other plant oils known to supply the unsaturated fatty acids as well as fuel.

On low cholesterol diets the eggs are limited to two a week. One pint of low fat skimmed milk or buttermilk is used daily. Protective foods included are green leaves, highly pigmented green and yellow vegetables, deeply colored fruits, citrus fruits, other fruits and vegetables, potatoes, legumes (dried beans, peas, lentils, garbanzas), nuts (Brazil nuts, almonds, peanuts, pine nuts, other nuts), protein rich sources of high biologic efficiency, low in animal fat, suggested previously, in addition to the foods included here; whole grain cereals with bran and germ proteins, which exhibit supplementary protein action; egg whites, in cooked dishes.

Caution on low fat diets is placed on securing sufficient fat-soluble vitamins. Vitamin A from plant sources comes chiefly from fortified margarine, crptoxantine as found in yellow corn, carotene (the provitamin A) occurring chiefly in green leafy plants such as kale, escarole, chard, beet greens, broccoli, yellow squash, carrots, sweet potatoes, apricots, and yellow fleshed peaches.

Fat soluble vitamins in the D group are not present in high concentrations in plant sources; there are more than 130 compounds with vitamin E activity, so this vitamin is fairly widely distributed—it is found in wheat germ oil, vegetable oils except olive oil, green leaves, and a small amount in oranges, bananas and lean meat; Vitamin K is chiefly confined to plant sources.

Low cost food stores for geriatric feeding for one week include:

- 5¼ quarts skimmed or buttermilk.
- 8 ounces dry beans, lentils, peas, or nuts.
- 3 pounds 7 ounces potatoes
- 1 pound 9 ounces green leaves, green or yellow vegetables.
- 2 pounds 6 ounces other fruits and vegetables.
- 1 pound 10 ounces tomatoes and citrus fruits.
- 2 eggs.
- 1 pound 12 ounces lean meat, fish, but no rabbit or fowl high in cholesterol or use instead protein alternates.
- 4 pounds 4 ounces bread, breakfast foods, grains of the whole grain type.
- 4 ounces wheat germ or corn germ or dried brewer's yeast or non-fat milk solids to replace the protein carried by a higher quota of eggs on ordinary diets.
- 4 ounces plant fats, enriched margarine, or equivalents in vegetable oils.
- 11 ounces sugars and syrups.

Such a dietary plan will provide daily: 2000 calories, 60 gm. protein from sources of high biologic efficiency, .68 gm. calcium, 1.32 gm. phosphorus, 12 mg. iron, 2 mg. copper, 5,000 I.U. Vitamin A group, 1.1 mg. thiamin, 2 mg. riboflavin, 12 mg. niacin, 75 mg. Vitamin C, and some other water soluble and fat soluble vitamins.

A low cholesterol meal pattern would be:

Breakfast—Fruit, fruit juice, whole grain cereals, skim milk. Variation: twice a week an egg or alternate.

Noon—Cottage cheese, farmer's style, or other protein-rich dishes with legumes, nuts, soybean curd, or cheese; cooked colored vegetable; other fresh vegetable, raw or cooked; whole grain bread or cooked whole rice; plant table fat; skimmed milk in soup or as a beverage.

Night—Protein-rich main dish equivalent to lean cooked muscle cuts of beef, lamb, veal, or fish, including skim milk Jack cheese, soybean products, legumes properly cooked, nuts, and cereal germ dishes; potato; green leaves or highly pigmented food; fruit for dessert or as a salad; plant table fat for seasoning.

Summary

1. A low cholesterol diet is favorably looked upon for geriatric feeding. Such a diet can be achieved by limiting eggs and whole milk, glandular cuts of meat, and all animal fat. A total of 100 to 200 mg. of cholesterol a day is allowed from food ingesta.

2. The other nutritional needs of the patient must be met and the other prevailing influences on the nutritional state are to be carefully considered.

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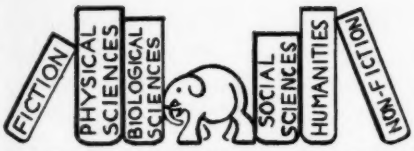
CORRECTION

The author of the Gerontologic Review "Connective Tissue Changes with Aging," which appeared in the October, 1947, issue, was listed as Harrison F. Ward instead of Harrison F. Wood.



BOOKS

PSYCHOSOMATIC PROBLEMS

CHRONIC DISEASE AND PSYCHOLOGICAL INVALIDISM, A PSYCHOSOMATIC STUDY, Jurgen Ruesch, The American Society for Research in Psychosomatic Problems, New York, 1946, $3.00, 191 pages.

In this monograph the authors report the results of an investigation into the psychologic characteristics of patients who tended to have either prolonged periods of convalescence or invalid reactions. Two groups of patients were studied. The first group consisted of 123 patients, who were seen for approximately three hours each. Another group of 64 patients was studied intensively while living in the hospital.

The time spent with each patient of this group varied from ten to fifty hours. All the patients were seen first in the University of California Hospital or Outpatient Clinic. Referral to the investigators took place either "because the patient did not recover quickly or because the patient was believed to be suffering from a psychoneurosis." All psychoneuroses and psychoses without physical symptoms and psychoneuroses never treated for physical symptoms were excluded from the study.

After a complete medical, surgical, or obstetrical workup in the corresponding departments of the hospital, each patient in the study was given a diagnostic, psychiatric interview for the purpose of establishing the nature of the patient's psychiatric disorder and the plan of treatment. This interview provided material for making ratings of adjustment, social class membership, social mobility, and a tabulation of the number and type of complaints. Patients were also given a shortened form of the Wechsler-Bellevue Intelligence Test, an abbreviated form of the Minnesota Multiphasic Personality Inventory, and a multiple choice Rorschach Test.

In addition to these tests, the 64 hospital patients were studied for periods of weeks and months. These patients were subjected to intensive individual and group psychotherapy, and information concerning their character structure was given special attention. Except for their willingness to stay in the hospital, these patients represented an unselected sample taken from the outpatient group. Special attention was devoted to the character problems of these patients and to their outstanding needs and fundamental conflicts seen in the light of childhood events.

From their observations, the authors conclude that patients showing delayed recovery are characterized by an absence of overt misbehavior or conduct disorders. Instead, maladjustment was expressed in terms of disease or sexual and marital difficulties. Analysis of the Rorschach and personality inventory scores indicated a high incidence of hypochondriacal, hysterical, and depressive trends among the patients showing delayed recovery.

The authors express surprise to discover that the symptomatology of these patients coincided in frequency and nature with that found in the psychoneurosis. The source of this surprise on the part of the authors is difficult to understand since the patients studied were referred to the authors because the examining physician believed the patient was suffering from psychoneurosis. For the same reason, it is not difficult to understand why pain in a variety of places, gastro-intestinal symptoms, and anxiety features were found in 91 per cent of the cases.

Analysis of the social data showed that a large proportion of the cases with delayed recovery belonged to the lower middle class. The authors believe that since the main feature of the lower middle class ideology is the importance of conformance with popular ideas and beliefs, members of this group are limited in the ways in which they can properly express their aggressive tendencies. Protracted illness thus becomes one of the acceptable ways in which persons of this class can avoid facing reality. Illness also provides contacts with members of a higher social group (doctors and nurses) and gives the patient added advantages of protection and care.

A total of 53 patients were studied to determine the possibilities for cure and to relate these to the actual therapeutic results obtained. The group with unfavorable prognosis gave significantly higher scores in the psychotic and psychopathic scales of the Minnesota Multiphasic Personality Inventory. The Rorschach Test did not prove of value in differentiating prognostically favorable from unfavorable cases.

Three types of therapeutic methods were used in the rehabilitation of cases with delayed recovery. The first method of psychologic advice, which was limited to three or four sessions, was effective only when traumatic psychologic experiences coincided with disease or when an accident led to the discovery of a pre-existing disease. The second method, which involved twenty to thirty sessions of individual psychotherapy, was more suitable for the patient with education limited to high school and with an I.Q. not exceeding 110. The authors believe that this type of therapy has a wide field of application. It is the ideal method of helping a patient over an acute phase of maladjustment primarily involving conflicts between the individual and his environment. The third method, group therapy in conjunction with individual therapy, was found of value.

A serious limitation in interpretation of this study is the lack of an adequate control group. Although some of the variables such as marital status, national stock, educational level, and occupational status are related to the general population in California, the more important differences found in this group are not compared with patients from the same hospital who showed a satisfactory rate of recovery. Thus, it may be that many of the characteristics regarded as significant, such as social status and social mobility, were common to all patients who turn to the University of California Hospital for medical care.

Since many cases of chronic disease have their origin in delayed recovery, the methods and results obtained in this study should be of interest to all those concerned with the care of the aged. The concept that complaints and symptoms are in part the result of the individual's deliberate selection and reinforcement of peripheral stimuli may be a useful guide in dealing with elderly patients.

N. W. SHOCK

A BRITISH SURVEY OF THE PROBLEMS OF THE OLD

OLD PEOPLE. Report of a Survey Committee on the Problems of Ageing and the Care of Old People (under the chairmanship of B. Seebohm Rowntree). Published for the Trustees of the Nuffield Foundation by Geoffry Cumberlege, Oxford University Press, London 1947, price 3s 6d., 203 pages.

This stimulating report interprets the results of a number of simultaneous studies dealing with different aspects of the old age problem. In seven brief chapters, totaling a little over 100 pages, the question of income of the old, of housing and living conditions, of homes and institutions, of recreation, and of employment are dealt with competently. An introductory chapter outlines the terms of reference, the scope of the study as well as its limitations, and the methodology employed.

The Committee members have undertaken

personal investigations in various parts of Great Britain, with emphasis on institutional provisions. They also planned and directed a considerable number of field surveys carried on by teams of investigators, carefully selected and trained. They interviewed well over 2,000 old people in six different areas. Summaries of the field surveys, in addition to some statistical material and pictures, will be found in the fifteen appendices of the report, covering roughly another 100 pages.

A well-qualified medical subcommittee considered directions in which research into the process of aging is or might be conducted. On behalf of the Foundation it reviewed applications for grants-in-aid and formulated a policy concerning future studies. Its recommendation for the promotion of further research and a suggested classification of problems in gerontology will also be of interest in this country (pages 108-109).

The entire report is written in the form of numbered paragraphs, many containing specific recommendations and estimates for the desirable extension of community facilities. The recommendations are practical and realistic. They are not afraid of value judgments, such as Statement 127: "In sickness or infirmity old people undoubtedly become a burden. They are not necessarily one that is resented; but a burden cheerfully borne still remains a burden." (page 47).

Among the conclusions and recommendations of the final chapter a word of caution has been inserted. Benefits paid to old people, from whatever source, absorb a certain proportion of the available and currently produced wealth of the country. While the Committee members express full sympathy with the widespread desire to be generous to the aged, they wish to support Lord Beveridge's words, "It is dangerous to be in any way lavish to old age until adequate provision has been assured for all vital needs, such as the prevention of disease and the adequate nutrition of the young." (page 95).

However, the Committee also states that it has found no acute poverty among the aged although a considerable measure of austerity. "Flexible Administration" of the Assistance Board has been "markedly successful" in adjusting benefits to needs in a humane but not unreasonably extravagant manner . . . "the Assistance Board's officers have also by their advice and guidance, contributed greatly to the welfare of the pensioners with whom they have come into contact." (page 99.)

The Committeee welcomes the free spectacles, dentures, hearing aids, and other medical appliances which will become available under the National Health Service and will particularly benefit old people (page 99). On the other hand, the Committee's visits to a number of institutions "have confirmed the widely held view that in the majority of them, the structure, equipment and regulations are unsuited to the needs of most old people." (page 99). The Committee favors the development of additional homes by public and voluntary agencies so as to accommodate "the vast number which are now seeking but unable to find admission." These homes are visualized as small units, averaging 30 to 35 residents. "It must be realized that the number of homes required over a period of the next fifteen or twenty years will total several thousand. All local authorities should give urgent attention to the matter." (page 100).

In the area of voluntary agencies the Committee found much to be done: "The administration of many charities needs to be overhauled; many trust deeds need to be altered to allow the trustees wider scope; in many institutions, particularly in the case of parochial charities, groups of charities should be combined . . . The whole picture is one of chaos and of frustration of the spirit in which the charities were originally endowed." (page 98).

The Committee recommends the provision and maintenance of an administration and training center, specializing in progressive methods of caring for the infirm aged. It sees clearly the need for continued and systematic inquiry into all matters affecting the aged, anticipating increasingly strong politi-

cal influence of the old people, conflicting interests, and a risk that claims may be advanced "which cannot be met without detriment to the interests of the community as a whole." (page 103). The creation of a well-informed and well-balanced public opinion, more social and medical study, technical experimentation, and above all energetic action in introducing community facilities are recommended.

This very meaty and courageous report should be widely read in this country, although many of its specific recommendations are not applicable within the American setting. Basic human needs, basic trends, and the cultural lag of many of our social institutions are much alike.

HERTHA KRAUS

GERIATRIC CARE

MEDICAL ASPECTS OF GROWING OLD, A. T. Todd, M.D., Williams & Wilkins Co., Baltimore, 1946, $3.50, 164 pages.

Dr. Todd's book, couched in readable lay terminology, is a discussion of problems of old age with particular emphasis on the diet, digestive processes, and the management and care of the nose, skin, hair, and feet. Some space is accorded to a philosophic discussion of retirement to include the age of retirement, whether retirement should be compulsory or voluntary, and some of the sedentary employments and hobbies which an older person can assume upon retirement from his regular occupation. Physical exercises should be few and should be directed in such a manner as to place a minimum of strain on the cardio-vascular system.

An interesting element which is discussed is the problem of baths. The author feels that when baths are taken too frequently fats which must necessarily be replaced may be removed from the skin. Dilatation of blood vessels of the skin accompanying a hot bath may result in some diminution of blood supply to the internal organs which may already be compromised. On the other hand, a cold bath withdraws heat, and this heat must be replaced by breakdown in the source of energy of glycogen or animal products. Thus, strain will be thrown upon both food reserves and the enzyme system.

The importance of sleep is emphasized as an aid not only to the digestive system but also to the assimilation of food which has been ingested during the day. Methods on treatment of sleeplessness are discussed, and particular attention is paid to regular habits, comfortable bedding, and restful surroundings. Dr. Todd advises light, ample evening meals exclusive of fat and rich foods, and recession of fluids, particularly in older men who may be forced to rise several times nightly for the purpose of voiding. The author has great antipathy toward the use of sleeping drafts, sleeping tablets, and hypnotics and feels that many of these drugs act as systemic poisons.

Bowel regulation is largely achieved by correct, well-balanced diet and by exercises to tone the abdominal muscles and induce the return of assumption of normal bowel rhythm. Treatment and care of genito-urinary troubles in men is again purposed by correction of whatever errors of digestion or living are noted. Restrictions of fluid late in the day prior to bedtime may help the individual to a night of complete rest and sleep. The use of male hormone, testosterone or methyl testosterone, is suggested rather enthusiastically insofar as results which the author has achieved. If all this has failed, then the patient must choose whether he will consent to a prostatectomy or periodic catheterization. Dr. Todd states that the activity of the elderly man should be governed by his libido and potency.

Throughout the book one is struck by the attention which the author devotes to physi-

cal hygiene, correct diet, and proper mental hygiene. From the strictly scientific standpoint, many individuals may regard this book as platitudinous; but, to lay individuals in the decline of life it will provide not only an hour or two of interesting reading but also excellent advice on the regulation of their lives in order to glean the greatest degree of satisfaction and good health.

WILSON G. BROWN

BOOKS RECEIVED

Books received since September 1, 1947, are acknowledged in the following list. Insofar as space and time permit, some will be selected for review in a later issue, but it is unlikely that all will be reviewed.

Contemporary American Family, by Ernest R. Groves and Gladys H. Groves,. J. B. Lippincott Company, Chicago, 1947, $4.50, 838 pages.

Fatigue and Impairment in Man, by S. Howard Bartley and Eloise Chute, McGraw-Hill Book Co., New York, 1947, $5.50, 429 pages.

Lecciones de Geriatria, Enfermedades de la Vejez, volumes 1 and 2, by Prof. Dr. M. Beltrán Báguena, Librería de F. García Muñoz, Valencia, 1947, price, vol. I, 28 pesetas, vol. II, 35 pesetas, 267 pages, paper bound.

Non-cash Needs of Aged Persons Affecting Their Individual and Social Security, An Annotated Bibliography, by Florence A. Armstrong, Federal Security Agency, Social Security Administration, Bureau of Research and Statistics, Division of Coordination Studies, August, 1947, 199 pages.

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